

1 FOOD AND DRUG ADMINISTRATION

2 CENTER FOR DRUG EVALUATION AND RESEARCH

3
4
5 JOINT MEETING OF THE ANTI-INFECTIVE DRUGS AND
6 NONPRESCRIPTION DRUGS ADVISORY COMMITTEES

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9
10 Monday, April 2, 2012

11 8:00 a.m. to 4:30 p.m.

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14
15 DoubleTree by Hilton

16 Washington, D.C./Silver Spring

17 8727 Colesville Road

18 Silver Spring, MD
19
20
21
22

Meeting Roster

DESIGNATED FEDERAL OFFICER (Non-Voting)

Minh Doan, Pharm.D.

Division of Advisory Committee and Consultant

Management

Office of Executive Programs

CDER, FDA

ANTI-INFECTIVE DRUGS ADVISORY COMMITTEE MEMBERS

(Voting)

Diane Cappelletty, Pharm.D.

Associate Professor Pharmacy Practice

University of Toledo College of Pharmacy

Toledo, Ohio

1 **Sheldon L. Kaplan, M.D.**

2 Professor and Vice Chairman for Clinical Affairs

3 Head, Pediatric Infectious Disease Section

4 Department of Pediatrics

5 Baylor College of Medicine

6 Chief, Infectious Disease Service

7 Head, Department of Medicine

8 Texas Children's Hospital

9 Houston, Texas

10
11 **Thomas A. Moore, M.D., FACP**

12 ***(Chairperson)***

13 Chairman

14 Department of Infectious Diseases

15 Ochsner Health System

16 New Orleans, Louisiana

1 **Michael Neely, M.D.**

2 Assistant Professor

3 Department of Pediatrics

4 Keck School of Medicine

5 University of Southern California

6 Los Angeles, California

7
8 **Kathleen Young**

9 *(Consumer Representative)*

10 Executive Director

11 Alliance for Prudent Use of Antibiotics

12 Boston, Massachusetts

13
14 **NONPRESCRIPTION DRUGS ADVISORY COMMITTEE MEMBERS**

15 **(Voting)**

16 **Steven C. Curry, M.D.**

17 Director, Department of Medical Toxicology

18 Banner Good Samaritan Medical Center

19 Professor of Clinical Medicine

20 University of Arizona

21 Phoenix, Arizona

22

1 **Walid Gellad, M.D., M.P.H.**

2 Assistant Professor of Medicine

3 School of Medicine

4 Assistant Professor of Health Policy and

5 Management, Graduate School of Public Health

6 University of Pittsburgh

7 Staff Physician

8 Veterans Affairs Pittsburgh Healthcare System

9 Pittsburgh, Pennsylvania

10
11 **Winifred A. Landis, R.Ph., C.D.E.**

12 Pharmacist, CVS Pharmacy

13 Lafayette, Indiana

14
15 **Richard Neill, M.D.**

16 Vice Chair, Department of Family Medicine and

17 Community Health

18 University of Pennsylvania

19 Philadelphia, Pennsylvania

1 **Ruth M. Parker, M.D.**

2 Professor of Medicine and Public Health

3 Emory University School of Medicine

4 Atlanta, Georgia

5
6 **Marcus M. Reidenberg, M.D., FACP**

7 Professor of Pharmacology, Medicine, and

8 Public Health

9 Weill Cornell Medical College

10 New York, New York

11
12 **Norma Martínez Rogers, Ph.D., R.N., FAAN**

13 *(Consumer Representative)*

14 Professor

15 University of Texas Health Science Center at

16 San Antonio, Department of Family Nursing

17 San Antonio, Texas

1 **Leslie R. Walker-Harding, M.D.**

2 Chief, Division of Adolescent Medicine

3 Professor of Pediatrics

4 Seattle Children's Hospital

5 University of Washington

6 Seattle, Washington

7
8 **TEMPORARY MEMBERS (Voting)**

9 **Christopher Carpenter, M.D., FIDSA**

10 Fellowship Program Director and Attending Staff

11 Division of Infectious Diseases

12 Director, Antimicrobial Stewardship Program

13 William Beaumont Hospital

14 Royal Oak, Michigan

15
16 **Ruth S. Day, Ph.D.**

17 Director, Medical Cognition Laboratory

18 Duke University

19 Durham, North Carolina

1 **Brian Erstad, Pharm.D.**

2 Professor, Department of Pharmacy Practice &

3 Science

4 University of Arizona College of Pharmacy

5 Tucson, Arizona

6
7 **Baruch Fischhoff, Ph.D.**

8 Howard Heinz University Professor

9 Department of Social and Decision Sciences and

10 Department of Engineering and Public Policy

11 Carnegie Mellon University

12 Pittsburgh, Pennsylvania

13
14 **Robert Gray, Ph.D.**

15 Professor of Biostatistics

16 Department of Biostatistics

17 Harvard School of Public Health and

18 Department of Biostatistics and Computational

19 Biology

20 Dana-Farber Cancer Institute

21 Boston, Massachusetts

22

1 **Marie Griffin, M.D.**

2 Professor, Department of Preventive Medicine
3 Vanderbilt University Medical Center
4 Nashville, Tennessee

5
6 **Joan Hilton, Sc.D., M.P.H.**

7 Assistant Professor
8 University of California San Francisco
9 San Francisco, California

10
11 **Gavin Huntley-Fenner, Ph.D.**

12 Chief Executive Officer and Senior Advisor
13 Huntley-Fenner Advisors
14 Irvine, California

15
16 **Elaine Morrato, Dr.P.H., C.P.H.**

17 Assistant Professor, Department of Pediatrics
18 University of Colorado Denver
19 Aurora, Colorado

1 Christian Ockenhouse, M.D., Ph.D.

2 *(Patient Representative)*

3 Director, U.S. Military Malaria Vaccine Program

4 Walter Reed Army Institute of Research

5 Naval Medical Research Center

6 Silver Spring, Maryland

7
8 Allen Vaida, Pharm.D., FASHP

9 Executive Vice President

10 Institute for Safe Medication Practices

11 Horsham, Pennsylvania

12
13 Sidney Wolfe, M.D.

14 *(Consumer Representative to the Drug Safety and*

15 *Risk Management Advisory Committee)*

16 Director, Health Research Group

17 Public Citizen

18 Washington, District of Columbia

1 **T. Mark Woods, Pharm.D.**

2 Clinical Coordinator and Residency Program Director

3 Pharmacy Department

4 Saint Luke's Hospital

5 Kansas City, Missouri

6
7 **ACTING INDUSTRY REPRESENTATIVES TO THE COMMITTEES**

8 **(Non-Voting)**

9 **Patrick A. Robinson, M.D.**

10 *(Acting Industry Representative to the*

11 *Anti-Infective Drugs Advisory Committee)*

12 Deputy International Therapeutic Area Head-Virology

13 Boehringer-Ingelheim

14 Ridgefield, Connecticut

15
16 **Lorna C. Totman, Ph.D., DABT**

17 *(Acting Industry Representative to Nonprescription*

18 *Drugs Advisory Committee)*

19 Principal

20 Lorna Totman Consulting, LLC

21 Annandale, Virginia

22

1 **CENTERS FOR DISEASE CONTROL AND PREVENTION SPEAKER**

2 **(Non-Voting, Presenting Only)**

3 **Linda Neff, Ph.D., M.S.P.H.**

4 Senior Epidemiologist

5 Career Epidemiology Field Office

6 Office of Science and Public Health Practice

7 Office of Public Health Preparedness and Response

8 Centers for Disease Control and Prevention

9 Atlanta, Georgia

10
11 **DEPARTMENT OF HOMELAND SECURITY SPEAKER**

12 **(Non-Voting, Presenting Only)**

13 **Susan Collier-Monarez, Ph.D.**

14 Threat Characterization and Attribution

15 Branch Chief

16 Chemical and Biological Defense Division

17 Science and Technology Directorate

18 Department of Homeland Security

19 Washington, District of Columbia

1 **MINNESOTA DEPARTMENT OF HEALTH SPEAKER**

2 **(Non-Voting, Presenting Only)**

3 **Ruth Lynfield, M.D.**

4 State Epidemiologist and Medical Director

5 Minnesota Department of Health

6 St. Paul, Minnesota

7
8 **ASSOCIATIONS' SPEAKERS (Non-Voting, Presenting**
9 **Only)**

10 **Robert R. Bass, M.D., FACEP**

11 Executive Director

12 Maryland Institute for Emergency Medical

13 Services Systems

14 Chair, Committee on Prepositioned Medical

15 Countermeasures for the Public

16 Institute of Medicine

17 Baltimore, Maryland

1 **James S. Blumenstock**

2 Chief Program Officer

3 Public Health Practice

4 Association of State and Territorial

5 Health Officials

6 Arlington, Virginia

7
8 **Marcie Bough, Pharm.D.**

9 Senior Director, Government Affairs

10 American Pharmacist Association

11 Washington, District of Columbia

12
13 **John Bradley, M.D.**

14 Director, Division of Infectious Diseases

15 Rady Children's Hospital San Diego

16 Member, Anthrax Working Group, Disaster Planning

17 Advisory Council

18 American Academy of Pediatrics

19 San Diego, California

1 **Jack Herrmann, M.S.Ed., N.C.C.**

2 Senior Advisor & Chief

3 Public Health Preparedness

4 National Association of County and City

5 Health Officials

6 Washington, District of Columbia

7
8 **James J. James, M.D., Dr.P.H.**

9 Center for Public Health Preparedness and

10 Disaster Response

11 American Medical Association

12 Chicago, Illinois

13
14 **Andrew T. Pavia, M.D., FAAP, FIDSA**

15 George and Esther Gross Presidential Professor

16 Chief, Division of Pediatric Infectious Diseases

17 University of Utah

18 Member, Board of Directors and Chair,

19 Pandemic Influenza and Bioemergencies Task Force

20 Infectious Diseases Society of America

21 Salt Lake City, Utah

22

1 **Christopher J. Topoleski**

2 Director, Federal Regulatory Affairs American
3 Society of Health-System Pharmacists
4 Bethesda, Maryland

5
6 **FDA PARTICIPANTS (Non-Voting)**

7 **Edward Cox, M.D., M.P.H.**

8 Director
9 Office of Antimicrobial Products (OAP)
10 Office of New Drugs (OND), CDER, FDA

11
12 **Katherine Laessig, M.D.**

13 Deputy Director
14 Division of Anti-Infective Products (DAIP)
15 OAP, OND, CDER, FDA

16
17 **Andrea Leonard-Segal, M.D.**

18 Director
19 Division of Nonprescription Clinical Evaluation
20 ODE IV, OND, CDER, FDA

1 John Alexander, M.D., M.P.H.

2 Clinical Team Leader

3 DAIP, OAP, OND, CDER, FDA

4
5 Barbara Cohen, M.P.A.

6 Social Science Analyst

7 Division of Nonprescription Clinical Evaluation

8 ODE IV, OND, CDER, FDA

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P R O C E E D I N G S

Call to Order

Introduction of Committees

DR. MOORE: Good morning, everybody. I'm Dr. Moore, and wanted to just start the meeting this morning. Needless to say, if you've seen the agenda, an extraordinarily full docket. So in advance, what I'd like to say is I'm going to have to keep everybody on a tight leash so we can get done on time. The reason we want to get done on time, of course, is, I'm sure everyone here is going to be seeing the KU game tonight; KU beat Kentucky, of course.

[Laughter.]

DR. MOORE: It just goes without saying.

So we'll go ahead and get started.

I'd like to remind everybody present to please silence your cell phones, Blackberrys, and other devices if you have not already done so. Today's meeting is -- sorry. We're going to cover doxycycline medkits for public health preparedness for an anthrax attack.

1 Let me introduce ourselves before we get
2 started. So everybody's here. We'll get started.

3 Why don't we start by going around the table
4 and introducing ourselves?

5 Dr. Cox, why don't we start with you?

6 DR. COX: Good morning. Ed Cox, director of
7 the Office of Antimicrobial Products, CDER, FDA.

8 DR. LAESSIG: Hi. Katy Laessig, deputy
9 director, Division of Anti-Infective Products, FDA.

10 DR. ALEXANDER: John Alexander, medical team
11 leader in the Division of Anti-Infectives at FDA.

12 DR. LEONARD-SEGAL: Good morning. Andrea
13 Leonard-Segal. I direct the Division of
14 Nonprescription Clinical Evaluation at FDA.

15 MS. COHEN: Good morning. Barbara Cohen,
16 social science analyst, Division of Nonprescription
17 Clinical Evaluation, FDA.

18 DR. GRIFFIN: Marie Griffin, internist and
19 pharmacoepidemiologist from Vanderbilt.

20 DR. ERSTAD: Brian Erstad, professor at the
21 University of Arizona.

22 DR. DAY: Ruth Day, director of the medical

1 cognition laboratory at Duke University.

2 DR. GRAY: Robert Gray, professor of
3 biostatistics at Harvard School of Public Health in
4 Dana-Farber Cancer Institute.

5 DR. WOODS: Mark Woods, coordinator of
6 clinical pharmacy services and residency program
7 director at St. Luke's Hospital in Kansas City,
8 Missouri.

9 DR. MORRATO: Good morning. I'm Elaine
10 Morrato. I'm an epidemiologist in the department
11 of health systems management and policy at the
12 Colorado School of Public Health.

13 DR. CARPENTER: Good morning. Chris
14 Carpenter. I'm an infectious disease specialist in
15 Beaumont Hospital in Michigan.

16 DR. CURRY: Steven Curry, medical
17 toxicology, Phoenix, Arizona, University of Arizona
18 College of Medicine.

19 DR. REIDENBERG: I'm Marcus Reidenberg. I'm
20 a clinical pharmacologist at Weill Cornell.

21 DR. NEILL: Richard Neill. I'm a family
22 physician from the University of Pennsylvania, a

1 graduate of the University of Kentucky, 1982, and
2 1986-present. December 10th, 1978, Kansas lost to
3 Kentucky after blowing a seven-point lead with a
4 minute and 36 seconds left in the game.

5 MS. YOUNG: Kathy Young with the Alliance
6 for Prudent Use of Antibiotics. I'm a public
7 policy specialist.

8 DR. DOAN: Minh Doan, designated federal
9 officer.

10 DR. MOORE: Tom Moore, chairman of
11 infectious diseases at Ochsner Medical Center in
12 New Orleans and a recent mover to New Orleans.

13 DR. NEELY: I'm Michael Neely. I'm a
14 specialist in pediatric infectious diseases and
15 pharmacology at the University of Southern
16 California in Los Angeles.

17 DR. CAPPELLETY: Diane Cappelletty,
18 associate professor of pharmacy at the University
19 of Toledo, Toledo, Ohio.

20 DR. KAPLAN: Shelly Kaplan. I'm a pediatric
21 infectious diseases physician at Baylor College of
22 Medicine and Texas Children's Hospital in Houston.

1 DR. WOLFE: Ruth Parker, Emory University
2 School of Medicine, professor of medicine,
3 pediatrics, and public health, strong opponent of
4 Kentucky. And I'll try not to let that bias my
5 opinion today.

6 [Laughter.]

7 MS. LANDIS: Good morning. Winnie Landis,
8 community pharmacist and diabetes educator from
9 Lafayette, Indiana.

10 DR. GELLAD: Walid Gellad, primary care
11 physician and health services researcher at the
12 University of Pittsburgh and Pittsburgh VA.

13 DR. WALKER-HARDING: Leslie Walker-Harding.
14 I'm professor of pediatrics and chief of division
15 of adolescent medicine at the University of
16 Washington and Seattle Children's.

17 DR. HUNTLEY-FENNER: Gavin Huntley-Fenner.
18 I am a brain and cognitive scientist joining you
19 here from the FDA's Risk Communication Advisory
20 Committee.

21 DR. WOLFE: Sid Wolfe, internist with the
22 Health Research Group of Public Citizen.

1 DR. HILTON: Joan Hilton, biostatistician at
2 UC San Francisco.

3 DR. OCKENHOUSE: Good morning. I'm Chris
4 Ockenhouse. I'm an infectious disease officer at
5 the Walter Reed Army Institute of Research. I'm
6 here representing patient representative.

7 DR. VAIDA: Good morning. Allen Vaida,
8 executive vice president at the Institute for Safe
9 Medication Practices. I'm a pharmacist.

10 DR. FISCHHOFF: I'm Baruch Fischhoff, former
11 chair of FDA's Risk Communication Advisory
12 Committee and a decision scientist at Carnegie
13 Mellon University, a Division III school.

14 [Laughter.]

15 DR. TOTMAN: Lorna Totman. I'm the acting
16 industry representative to the Nonprescription
17 Drugs Advisory Committee.

18 DR. ROBINSON: Patrick Robinson, the
19 industry representative to the Anti-Infective Drugs
20 Advisory Committee. I sit at Boehringer Ingelheim.
21 And we play hockey, not basketball.

22 DR. MOORE: Everyone's got their cross to

1 bear, I see.

2 So for topics such as those being discussed
3 at today's meeting, there are often a variety of
4 opinions, some of which are quite strongly held,
5 speaking about the anthrax business, not
6 basketball.

7 Our goal is that today's meeting will be a
8 fair and open forum for discussion of these issues
9 and that individuals can express their views
10 without interruption. Thus, as a gentle reminder,
11 individuals will be allowed to speak into the
12 record only if recognized by the chair. We look
13 forward to a productive meeting.

14 In the spirit of the Federal Advisory
15 Committee Act and the Government in the Sunshine
16 Act, we ask that the advisory committee members
17 take care that their conversations about the topic
18 at hand take place in the open forum of the
19 meeting. We are aware that members of the media
20 are anxious to speak with the FDA about these
21 proceedings. However, FDA will refrain from
22 discussing the details of this meeting with the

1 media until its conclusion.

2 For the convenience of the media
3 representatives, I would like to identify the FDA
4 press contact, Yolanda Fultz-Morris.

5 Hi. Thank you for standing.

6 Also, the committee is reminded to please
7 refrain from discussing the meeting topic during
8 breaks or lunch. Thank you.

9 I want to welcome everybody to this meeting
10 and now will pass to Minh Doan, who will read the
11 conflict of interest statement.

12 **Conflict of Interest Statement**

13 DR. DOAN: The Food and Drug Administration
14 is convening today's meeting of the Joint Meeting
15 of the Anti-Infective Drugs Advisory Committee and
16 the Nonprescription Drugs Advisory Committee under
17 the authority of the Federal Advisory Committee Act
18 of 1972. With the exception of the industry
19 representative, all members and temporary voting
20 members of the committees are special government
21 employees or regular federal employees from other
22 agencies and are subject to federal conflict of

1 interest laws and regulations.

2 The following information on the status of
3 this committee's compliance with federal ethics and
4 conflict of interest laws, covered by but not
5 limited to those found at 18 U.S.C., Section 208
6 and Section 712 of the Food, Drug, and Cosmetic
7 Act, is being provided to participants in today's
8 meeting and to the public.

9 FDA has determined that members and
10 temporary voting members of the committees are in
11 compliance with the federal ethics and conflict of
12 interest laws. Under 18 U.S.C., Section 208,
13 Congress has authorized FDA to grant waivers to
14 special government employees and regular federal
15 employees who have potential financial conflicts
16 when it is determined that the agency's need for a
17 particular individual's services outweighs his or
18 her potential financial conflict of interest.

19 Under Section 712 of the Food, Drug, and
20 Cosmetic Act, Congress has authorized FDA to grant
21 waivers to special government employees and regular
22 federal employees with potential financial

1 conflicts when necessary to afford the committees
2 essential expertise.

3 Related to the discussion of today's
4 meeting, members and temporary voting members of
5 the committees have been screened for potential
6 financial conflicts of interest of their own, as
7 well as those imputed to them, including those of
8 their spouses or minor children, and, for purposes
9 of 18 U.S.C. Section 208, their employers. Their
10 interests may include investments, consulting,
11 expert witness testimony, contracts, grants,
12 CRADAs, teaching, speaking, writing, patents and
13 royalties, and primary employment.

14 Today, the committees will provide advice on
15 types of consumer studies needed to assess proper
16 use of a medkit containing doxycycline, to be taken
17 in the event of anthrax exposure. Issues such as
18 feasibility of an FDA-approved medkit as a public
19 health strategy, the role of personal medkits, home
20 stockpiling, and interfaces of home readiness with
21 public health systems will be raised in the course
22 of the discussions.

1 The Biomedical Advanced Research and
2 Development Authority will propose a possible plan
3 for a step-wise development program for medkits
4 containing oral doxycycline hyclate.

5 This is a particular matters meeting during
6 which general issues will be discussed. A copy of
7 this statement will be available for review at the
8 registration table during the meeting and will be
9 included as part of the official transcript.

10 To ensure transparency, we encourage all
11 standing members, committee members, and temporary
12 voting members to disclose any public statements
13 that they have made concerning the topic at issue.

14 With respect to FDA's invited industry
15 representatives, we would like to disclose that
16 Drs. Patrick Robinson and Lorna Totman are
17 participating in this meeting as non-voting
18 industry representatives, acting on behalf of
19 regulated industry. Drs. Robinson and Totman's
20 role at this meeting is to represent industry in
21 general and not any particular company.

22 Dr. Patrick Robinson is employed by

1 Boehringer Ingelheim Pharmaceuticals. Dr. Lorna
2 Totman is principal at the Lorna Totman Consulting,
3 LLC, and also an associate member of the Consumer
4 Healthcare Products Association and provides
5 consulting services to the association.

6 With regard to FDA's guest speakers, the
7 agency has determined that the information to be
8 provided by these speakers is essential. The
9 following interests are being made public to allow
10 the audience to objectively evaluate any
11 presentation and/or comments made by the speakers.

12 Dr. James [sic] Bradley has acknowledged
13 that his employer has contracts for two studies
14 with the drug moxifloxacin. Dr. Bradley is a site
15 principal investigator for one of studies and does
16 not receive personal reimbursement. As a guest
17 speaker, Dr. Bradley will not participate in
18 committee deliberations, nor will he vote.

19 We would like to remind members and
20 temporary members that if the discussions involve
21 any other products or firms not already on the
22 agenda for which an FDA participant has a personal

1 or imputed financial interest, the participants
2 need to exclude themselves from such involvement,
3 and their exclusion will be noted for the record.
4 Thank you.

5 DR. MOORE: Thank you, Minh.

6 We had Dr. Rogers join us.

7 Dr. Rogers, sorry. We went around the room
8 and introduced ourselves. If you would be so kind
9 as to do that for us and read it into the record,
10 that would be great.

11 DR. ROGERS: Dr. Norma Rogers. I'm from UT
12 Health Science Center, and I'm a consumer
13 representative.

14 DR. MOORE: Thank you very much.

15 We're going to pass the baton over to
16 Dr. Andrea Leonard-Segal for a plaque presentation.

17 DR. LEONARD-SEGAL: Good morning. On behalf
18 of FDA, it is my pleasure to take this moment to
19 recognize three members of the Nonprescription Drug
20 Advisory Committee, whose terms expire in May. So
21 I'm going to first call up Dr. Curry.

22 Dr. Curry has served on the NDAC since March

1 2009. He's the director of the Department of
2 Medical Toxicology at Banner Good Samaritan Medical
3 Center. He's also a professor of medicine at the
4 University of Arizona College of Medicine and chief
5 of the toxicology section at Phoenix Children's
6 Hospital.

7 During his years on the committee, Dr. Curry
8 has made valuable contributions to the discussions
9 that have been helpful to the regulatory process.
10 In appreciation of his services, the FDA would like
11 to recognize Dr. Curry's service with this plaque.

12 The plaque says, "Advisory Committee Service
13 Award, presented to Steven C. Curry, M.D., in
14 recognition of distinguished service to the people
15 of the United States of America."

16 Thank you, Dr. Curry.

17 [Applause.]

18 DR. LEONARD-SEGAL: Winnie Landis.

19 Ms. Winifred Landis has served on the NDAC
20 since March 2009. She's a pharmacist with CVS
21 Pharmacy and a certified diabetes educator. Her
22 insights into OTC consumers have enriched the

1 advisory committee discussions. In appreciation of
2 her services, the FDA would like to recognize
3 Ms. Landis's service with this plaque. And the
4 plaque reads the same as Dr. Curry's.

5 Thank you very much.

6 [Applause.]

7 DR. LEONARD-SEGAL: Dr. Walker-Harding.

8 Dr. Leslie Walker-Harding has served on the
9 NDAC since March 2009. Dr. Walker-Harding is a
10 professor in the Department of Pediatrics at the
11 University of Washington and affiliate faculty in
12 the School of Public Health, Maternal and Child
13 Public Health. In addition, she is chief of the
14 adolescent medicines division at Children's
15 Hospital and Regional Medical Center and co-
16 director of the Adolescence Substance Abuse Program
17 at Seattle Children's Hospital.

18 Dr. Walker-Harding's expertise has been very
19 valuable in enhancing the discussions and
20 deliberations of the Nonprescription Drug Advisory
21 Committee. In appreciation of her services, the
22 FDA would like to recognize Dr. Walker-Harding's

1 service with this plaque. And it reads the same as
2 the other two.

3 Thank you.

4 [Applause.]

5 DR. MOORE: Thank you very much.

6 So why don't we start now with the FDA
7 presentations? Dr. John Alexander will be
8 starting.

9 **FDA Presentation - John Alexander**

10 DR. ALEXANDER: Good morning. My name is
11 John Alexander, and I'm going to provide a little
12 bit of some introductory comments and a bit of
13 regulatory background for the doxycycline medkit.

14 So as an outline, I'm going to talk a little
15 bit first about the history of doxycycline, talk
16 about the proposal for the medkit itself, go
17 through a few regulatory issues with a doxycycline
18 medkit, talk a little bit about formulations, and
19 then go through today's agenda and the committee
20 questions.

21 So doxycycline is a tetracycline-class
22 antibacterial drug. It was first approved in 1967

1 for a variety of infections. Since its approval,
2 it largely replaced the use of older tetracyclines
3 because of a favorable pharmacokinetic profile that
4 allowed for once- or twice-daily dosing versus a
5 higher dose of the older tetracyclines that would
6 need to be given four times daily.

7 Pertinent to today's discussion about the
8 use of a doxycycline medkit, in 2001, there was a
9 Federal Register notice for doxycycline and
10 penicillin G procaine. This Federal Register
11 notice clarified that the existing indication for
12 anthrax included inhalational anthrax post-exposure
13 to reduce the incidence or progression of disease,
14 following exposure to aerosolized *Bacillus*
15 anthracis.

16 Now, with the publication of this Federal
17 Register notice, it basically meant that
18 manufacturers were allowed to submit labeling
19 supplements to include this indication in their
20 labeling for the doxycycline and penicillin G
21 procaine products.

22 About a year prior to the publication of

1 this Federal Register notice, ciprofloxacin was
2 also approved for a similar indication for
3 inhalational anthrax post-exposure.

4 For all three drugs, the basis of this
5 indication was the results of animal model studies
6 in rhesus macaques that showed that when any one of
7 these drugs was given to animals who were exposed
8 to Bacillus anthracis spores, that the treatment
9 with these antibacterial drugs was able to reduce
10 the development of anthrax disease and mortality in
11 the animals in comparison to a placebo.

12 So then, a little bit about the doxycycline
13 medkit. What we're here today to discuss is a
14 development program being proposed by BARDA. The
15 concept for the doxycycline medkit, as it currently
16 stands, is that a 10-day supply of doxycycline
17 would be available for home storage in the case of
18 an anthrax attack. The proposal would be that the
19 product would be made available for sale by
20 prescription.

21 Now, the development program itself is still
22 in its early stages. And so part of the reason for

1 bringing it to the advisory committee today is to
2 get advice on the development program. Ultimately,
3 though, BARDA would expect that if the doxycycline
4 medkit were to move forward, private manufacturers
5 would be contracted for production and distribution
6 of these medkits.

7 Now, we do have some experience with the use
8 of doxycycline medkits. The CDC was the sponsor of
9 an IND for a pilot study of the medkits that was
10 conducted in St. Louis. In one of the
11 presentations later this morning, you'll hear a
12 little bit more about the pilot study that was
13 conducted.

14 Doxycycline medkits were also made available
15 to postal workers in Minneapolis, Minnesota through
16 an emergency-use authorization. And the Minnesota
17 Department of Health will be making a presentation
18 later this morning to talk a little bit about that
19 experience with monitoring the use of the
20 doxycycline medkits in that population.

21 Now moving on into the regulatory issues,
22 were the doxycycline medkit to be approved, it's

1 expected that it would be approved through the
2 standard approval process for new drug products,
3 meaning that there would need to be substantial
4 evidence of the safety and effectiveness of the
5 doxycycline medkit in its intended use for home
6 storage.

7 I would also make a note that FDA does have
8 authorities to, in some instances, require
9 post-marketing studies or also has authority for
10 making further post-marketing requirements, though
11 I'd note that these are usually on the basis of
12 significant safety concerns.

13 I also wanted to talk a little bit about the
14 level of evidence required for emergency-use
15 authorization of drugs, although I would note at
16 this point, that this really isn't a mechanism that
17 would be thought of for making the doxycycline
18 medkits available by prescription.

19 An emergency-use authorization is when it's
20 reasonable to believe that a product may be
21 effective in treatment of a serious or life-
22 threatening condition; the known and potential

1 benefits outweigh the known and potential risks;
2 there are no adequate approved or available
3 alternatives. It's usually thought of within the
4 setting of an emergency scenario, which may include
5 widespread exposure.

6 Through the authorization, FDA can also
7 apply certain conditions of use. In the example of
8 the doxycycline medkit for postal workers, for
9 instance, the EUA authorization applied certain
10 conditions with regard to monitoring the
11 distribution of the kits, as well as collecting the
12 kits that were expired and replacing them.

13 So FDA has previously provided advice to
14 BARDA with regard to the development of a
15 doxycycline medkit. This advice fell into two
16 categories, one with regard to home medkit labeling
17 and packaging.

18 FDA identified the need for information with
19 regard to the ability of individuals to keep a
20 medkit intact and unused within their household, to
21 be able to locate the medkit within the household,
22 and to get information about the attitudes and

1 beliefs about the medkit. Our advice previously
2 noted that some of this information could
3 potentially come from the CDC study that you'll
4 hear about later.

5 FDA also advised on the conduct of labor and
6 comprehension studies in order to refine the
7 labeling of the medkit and actual-use studies. And
8 after my presentation is done, you'll hear from
9 Barbara Cohen from the Division of Nonprescription
10 Clinical Evaluation, who's going to give a
11 presentation about these types of studies that are
12 used typically for the over-the-counter products,
13 because we think they may be useful with regard to
14 looking at the home storage of doxycycline.

15 FDA also advised that the development of
16 specific public service announcements, with regard
17 to how the people would be informed about the need
18 to use the medkit, would also be useful.

19 Separate advice from the FDA also was
20 provided on home preparation crushing instructions
21 for the use of the doxycycline tablets in
22 individuals who could either not swallow the pills

1 or for partial doses, such as would be needed for
2 children. These instructions should be consumer
3 friendly, clear, straightforward, easy to read and
4 understand.

5 In order to evaluate the home preparation
6 instructions, the palatability of the mixture of
7 doxycycline with certain food substances was
8 needed. In addition, there would need to be
9 studies performed by laboratory personnel and also
10 volunteers from the general population. Those
11 studies would be intended to evaluate the ability
12 of people to adhere to the instructions, as well as
13 to study dose uniformity, dose recovery, and
14 stability of the doxycycline in these food
15 mixtures.

16 Those studies could then be used to
17 determine whether revisions to the procedures
18 and/or instructions would be required. In
19 addition, we also noted that bioequivalence or
20 bioavailability of the doxycycline preparations
21 using the proposed food substances might be needed
22 in certain instances.

1 Moving onto formulation, the proposal for
2 the doxycycline medkit is that it would contain
3 100-milligram tablets, but I would note that there
4 are multiple oral formulations of doxycycline that
5 are available. There are both tablets and capsules
6 available in different strengths, 50, 75,
7 100 milligrams.

8 There are other delayed-release and
9 extended-release products. There's a doxycycline
10 calcium syrup that's available as an oral
11 suspension of 50 milligrams per 5 mL. There's a
12 doxycycline monohydrate powder that's available to
13 create an oral suspension, and that's 25 milligrams
14 per 5 mL.

15 One of the questions that we're discussing
16 later was with regard to the formulation that
17 should be used within the doxycycline medkit. Some
18 considerations that need to apply for this would be
19 considerations about the shelf life and the
20 storage. For instance, the tablets have a shelf
21 life of at least approximately five years, as
22 opposed to the doxycycline syrup, which only has a

1 shelf life of about three years.

2 Palatability is another consideration. It
3 may be that the palatability of the oral suspension
4 powder or the syrup may be less than that of mixing
5 it with food, but that would be something that
6 would need to be evaluated.

7 The other question is with regard to the
8 ability to deliver effective doses, either through
9 crushing of the tablets and separating into doses
10 or through preparation of a doxycycline powder, if
11 that would be made available at home by parents.
12 The other consideration is for whether there are
13 other alternatives, such as lower strength,
14 chewable, or crushable tablet preparations that
15 might be useful in regard to dosing for children.

16 So as an overview of today's agenda, after
17 I'm done, you'll hear an overview of consumer
18 studies presented by Barbara Cohen. There will be
19 presentations from the CDC and the Minnesota
20 Department of Health on their experience with the
21 doxycycline medkits, a presentation from the
22 Department of Homeland Security with regard to the

1 assessment of the level of threat with regard to an
2 anthrax attack. BARDA is going to make a
3 presentation on the proposal for the doxycycline
4 medkit, and then there are the perspectives of
5 multiple and invited speakers that are going to be
6 given afterwards, along with an open public
7 hearing.

8 So in preparation for today's meeting, I
9 think it's always useful to go over the questions
10 that are going to be asked at the end of the day.
11 We're going to ask for the committee to please
12 comment on the public health implications of a
13 prescription doxycycline medkit intended for post-
14 exposure prophylaxis for an anthrax
15 counterterrorism event, specifically to address
16 potential benefits and risks if a prescription
17 medkit were approved with the intention of home
18 storage.

19 Please comment on additions or modifications
20 to the proposed and/or completed studies; for
21 example, labeling comprehension, palatability,
22 simulated use, or additional studies that would

1 help assess the risks and benefits.

2 What types of additional studies would be
3 helpful to assess how users would behave in a real-
4 life situation? What is a reasonable percentage of
5 study subjects who should understand various
6 components of the label and/or be able to refrain
7 from using the product for other uses?

8 The doxycycline medkit proposal includes
9 instructions for dosing children and adults who
10 cannot swallow pills using the 100 milligram
11 tablets. Are the completed proposed studies
12 sufficient, or are there additional recommended
13 studies to evaluate dosing instructions in this
14 population?

15 Doxycycline is available in other dosages
16 and liquid formulations. I'll also ask that you
17 please discuss the pros and cons of home
18 preparation mixture versus other available
19 formulations for use in a medkit.

20 Finally, I'd like to acknowledge the members
21 of the review team within the Division of
22 Anti-Infective products, as well as the individuals

1 from the Office of Counterterrorism and Emergency
2 Coordination in the Division of Nonprescription
3 Clinical Evaluation, who contributed to both the
4 review of the IND, as well as the preparation and
5 planning for today's meeting. Thank you.

6 DR. MOORE: Thank you, Dr. Alexander.

7 Let's now go to Ms. Barbara Cohen.

8 **FDA Presentation - Barbara Cohen**

9 MS. COHEN: Good morning. Again, I'm
10 Barbara Cohen, social scientist at the Division of
11 Nonprescription Clinical Evaluation at FDA.

12 My objective here today, this morning, is to
13 provide an overview of the four different types of
14 consumer studies that we oversee, that are
15 conducted by our industry sponsors in support of
16 applications brought forward; and, in doing so,
17 provide you with a context, sort of a common
18 framework, for our follow-on discussions about
19 potential consumer behavioral research regarding
20 the medkit.

21 So as a backdrop, why do we actually need
22 consumer studies? Well, in the over-the-counter

1 world, it's to make sure that a non-prescription
2 drug can be used both safely and appropriately with
3 consumers without the involvement of that
4 intermediate healthcare provider. Typically, we
5 use these studies to look at over-the-counter
6 RX-to-OTC switches, new OTC indications, or new OTC
7 target markets.

8 Now, the medkit scenario is different. It's
9 a prescription product, but the reason I'm up here
10 today, as John alluded to, is that this product has
11 elements of an over-the-counter product because
12 it's to be used in an emergency situation where
13 there may not be other extensive, real-time sources
14 of information.

15 So potentially, something could occur and
16 people would not necessarily have access quickly to
17 their doctor or pharmacist to ask questions. And
18 so, essentially, the product would need to stand on
19 its own in terms of being able to convey
20 information about how to safely use this product
21 and appropriately do so.

22 So before I get into those studies, I just

1 want to get into the key, overarching research
2 questions that we're trying to address when we're
3 doing these four kinds of studies or one of several
4 of them. And those issues for us, in our
5 prescription world, are, can consumers accurately
6 self-diagnose? And what I'm referring to here is
7 do they understand the condition that's on the
8 product label and/or situation in the case of this
9 particular product? And do they understand if they
10 have that condition or with this product, if they
11 are in that situation?

12 The second question is can they
13 appropriately self-select? So even if they
14 understand what the condition is, do they know that
15 they can appropriately use the product based on
16 their own health circumstances? And finally, of
17 course, can they correctly self-medicate and use
18 the product in a home-use setting?

19 So there are four types of consumer studies
20 that we oversee: label comprehension, human
21 factors, self-selection, and actual use. Now, for
22 most products there are not necessarily all four

1 studies were conducted, but this is the order in
2 which they're usually conducted when they are
3 conducted. And it really depends on what the
4 clinical needs are, as determined by the clinical
5 team, as to the extent to which these studies are
6 conducted. So I'm going to provide you a brief
7 overview on each of them.

8 Now, in the OTC world, we're governed by the
9 regulation 21 Code of Regulations 330.10. And that
10 just states that the labels must be likely to be
11 read and understood by the ordinary individual,
12 including individuals of low comprehension under
13 customary conditions of purchase and use. So
14 that's kind of the framework for our work.

15 So as I said, label comp studies are ideally
16 the first study in a non-prescription drug
17 development program. They're kind of a necessary
18 component because, obviously, if people can't
19 understand the label, they're not necessarily going
20 to be able to use the product correctly. So I
21 would say it's a necessary, but not necessarily
22 sufficient research tool. And the study is

1 determined, in a nutshell, if a label, including
2 the package inserts, communicate important
3 information about the drug to consumers.

4 So in the OTC world, this is the typical
5 drug facts label, just a template that I've put up
6 here. And with this product, we're talking -- and
7 I know that you'll see this later in more detail.
8 But this is a prototype, a sample prototype.

9 So here, a label comp study might have
10 consumers look at the front of this label, the
11 front of the package, which would be the label, and
12 then the package insert. So there's something here
13 about how to mix the product for people who cannot
14 swallow or children. And there's a package insert
15 with more information about doxycycline in general.
16 So those are the kinds of things that might be
17 envisioned to be tested in a label comp study for
18 this.

19 The endpoints for all of our label comp
20 studies are based on the key communication elements
21 in the label that need to be understood. That is
22 the unique elements to the particular label in

1 question. And again, as I said, it's all grounded
2 in clinical rationale. But it's important to note
3 that these studies are testing only comprehension.
4 They're not designed to assess what consumers will
5 actually do once they have the product.

6 So just a couple of words about the
7 methodology. They're generally all-comers for
8 these studies. It's anybody in the U.S.
9 population, a representative sample, because
10 anybody could go into a drugstore and pick up an
11 OTC product. Likewise, anybody could potentially
12 ask their doctor for a prescription for a medkit.

13 The primary data collection tool is a
14 questionnaire with scripted interviews and with
15 various types of questions, usually close-ended,
16 yes/no; open-ended, why do you say that. And it's
17 based on a lot of scenarios, typically. So we give
18 the respondents a hypothetical medical situation,
19 and we're testing their ability to apply the
20 information from the label.

21 So for example, Janet's a 38-year-old with
22 diabetes who has a headache. Is it okay or not

1 okay for her to take the medication? That's after
2 they're given the label to read. And then, why do
3 you say that?

4 So for example, for this study, aspects that
5 these kinds of studies could address for this
6 product would be, will consumers understand,
7 obviously, the key aspects of the label, relating
8 to indication, dosing, length of therapy, and
9 warnings.

10 Another key issue might be, will they
11 understand that this is just a starter dose, and as
12 John said, it would be 10 days. They need to
13 visit, potentially, a public dispensing center to
14 obtain the full course of therapy. And you'll hear
15 more about that later.

16 The second kind of study that we often
17 oversee are human factor studies, and these can be
18 either part of a label comp study or a standalone,
19 separate study. They are typically conducted when
20 a product brings a new way of dosing administration
21 into the OTC arena. And the testing assesses -- I
22 mean, once we know that they understand the

1 directions on the label, we want to see whether
2 they actually can demonstrate that they can do it.

3 An active ingredient is usually not
4 administered in these studies, but typically what
5 we do is we bring people into -- these are not
6 human factor studies that you might think of
7 ordinarily. It's not in a laboratory or anything,
8 but with kind of very rigid scientific metrics.
9 But we bring people into a consumer research
10 facility. They are given the box, the product, and
11 maybe some things, utensils, or whatever. And we
12 just want to see what they do and if they can
13 really follow the directions correctly.

14 So for instance, a human factor study that
15 would be relevant in this case might be do they
16 understand it; can they demonstrate that they'll
17 understand the instructions for preparing the mix
18 for children and those who cannot swallow the
19 pills? And again, you'll see this later, I think
20 these are currently in this handout, in the
21 package.

22 So the next kind of study that is sometimes

1 conducted are self-selection studies. And as I
2 said, the objective with these is to determine if
3 consumers can appropriately self-select or not
4 select to use an OTC product. It's assessing the
5 ability of consumers to apply the drug labeling
6 information not to a third-party hypothetical like
7 we saw in the case of the diabetes for label comp,
8 but to their own personal health situation.

9 So when we require it in the OTC world would
10 be if there's a new OTC target population, or if a
11 product is contraindicated for a select population.
12 So we want to be certain that those individuals
13 won't use the product.

14 Typically, we try to be more -- or the
15 sponsor tries to be more efficient in terms of the
16 target population for these studies because we know
17 that not everybody would necessarily be a candidate
18 for product use. So they could look at potential
19 product uses in non-users or they might be looking
20 at people who should definitely just not use this
21 medication.

22 Again, these studies are really

1 designed -- they're very sort of individually
2 designed, and it's really based on the clinical
3 issues that the team determines with each
4 particular product.

5 So in this testing procedure, typically, the
6 participant reads the label, and then a typical
7 question might be, then, is it okay for you to use
8 and then why did you say that. And then on the
9 back end, so as not to bias them by thinking about
10 their medical issues up front, we collect their
11 demographic information and their medical history.

12 Correct self-selection is usually based on
13 the self-reported information, but occasionally
14 there might be medical diagnostic tests, lab tests,
15 that are conducted as well, again depending on what
16 the clinical issues are.

17 As with all the studies, the success
18 thresholds are based on this clinical rationale,
19 determined a priori. So, for example, one of the
20 ways that self-selection studies might be used for
21 this kit would be -- before you were taken into
22 actual use, which I'll get into in a minute. But

1 if you'd want to get some preliminary read, bring
2 consumers into a research facility, have them read
3 the package and then say, "If you had a tick bite,
4 would you use this product?

5 "If there was an anthrax attack in another
6 part of the world, would you use this product? If
7 there was something else, another kind of attack
8 that was closer to you, would you use this product?
9 If you had a bacterial infection, would you use
10 this," that kind of thing.

11 The final type of study that our industry
12 sponsors sometimes conduct is an actual-use study.
13 And what that is, that's generally the most complex
14 kind of initiative. And it's trying to simulate
15 the use of a product in a "real-world setting."
16 And as you can imagine, that's pretty difficult to
17 do. And so there are a lot of design issues with
18 them.

19 But just, in a nutshell, the primary
20 objectives of these studies usually are to see
21 whether people adhere to label directions and
22 warnings. And secondary objectives are sometimes

1 to provide safety data for the product, additional
2 safety data in an unsupervised setting.

3 So again, in the over-the-counter world, we
4 ask for them when there's a new or complicated
5 dosing regimen, when there's maybe a new method of
6 use of an OTC drug, et cetera. And again, the
7 population, as with all these other studies, except
8 for label comp, could be anybody who has an
9 interest in the product or could be populations of
10 interest only. The study length depends on the
11 labeled duration of use and the success threshold
12 as before.

13 So typically how these work is that
14 consumers are recruited through ads or flyers in
15 the drugstore, people who have that condition.
16 They go to the drugstore to pick up the product.
17 And then they have some medical screening or
18 whatever, if that's appropriate, but little
19 information about the product because we're trying
20 to simulate what it would be if they pick it up in
21 the drugstore.

22 Then they record their use in a diary,

1 either an electronic or paper diary, along with
2 their symptoms that caused them to use the product.
3 It could be concomitant medications or any other
4 things that we think are kind of important to know.
5 And then at the end of the study, they return the
6 diary and the unused product.

7 So you're going to hear more about,
8 actually, the CDC study. The St. Louis study,
9 which you're going to hear about in a minute, is
10 kind of an actual-use study. But some of the other
11 ways that actual-use studies could be applied in
12 this area are, again, one of the things that the
13 CDC study addressed was measurement of actually
14 non-actual use in this case. Will the consumers
15 leave the medkit intact in their home if there's no
16 anthrax event? You give it to them for a period of
17 time, and you see what happens.

18 Another way an actual-use study could be
19 used is, do they use it for potential Lyme disease
20 if they're in a high Lyme disease area, or do they
21 use it to self-medicate if they have a bacterial
22 infection, or if they have a cold, or something?

1 Finally, another potential use of this
2 methodology could be, give it to them -- and it
3 could be just placebo -- and tell them that at some
4 point in time -- could be three months, could be
5 three years -- there is going to be an emergency
6 fire drill. And it's going to say, "This is an
7 emergency test."

8 But they're going to have to see whether
9 they can locate their kit, whether they remember
10 where it is, and whether they have all the
11 necessary ingredients on hand in such a simulated
12 emergency because the mixing, again, for the
13 children and adults who cannot swallow, requires
14 certain ingredients to mix it in with.

15 So in conclusion, there are basically four
16 different types of consumer studies that I've
17 discussed, that we oversee: label comp, human
18 factors, self-selection, and actual use. Each
19 product that we look at is pretty individual and
20 has its own issues. And so there's some degree of
21 flexibility in terms of the issues that these can
22 address. But again, I just provide this to you as

1 food for thought. There may be issues that you
2 have that may need to be addressed by whole other
3 types of research.

4 So again, thank you for your time, and we're
5 very interested in hearing your feedback.

6 DR. MOORE: Thank you very much, Ms. Cohen.

7 So now we're going to hear from Dr. Neff
8 from the CDC by phone.

9 Are we ready to hear her disembodied voice?

10 DR. NEFF: I'm ready if you are.

11 DR. MOORE: Dr. Neff, is that you?

12 DR. NEFF: Yes. Can you hear me?

13 DR. MOORE: Yes, ma'am. I believe we can
14 all hear you. Go ahead.

15 **Presentation - Linda Neff**

16 DR. NEFF: Thank you.

17 Good morning, everyone. I am Linda Neff,
18 senior epidemiologist in the Office of Public
19 Health Preparedness and Emergency Response at the
20 Centers for Disease Control. I want to thank
21 Dr. Alexander and Barbara for a great introduction
22 and setup for the CDC medkit study. They gave a

1 great background.

2 Back in 2005, national leaders began
3 speaking and talking about robust strategies that
4 would be needed to assure the health and safety of
5 the American public against significant threats,
6 such as the release of anthrax. And this is
7 post-9/11 and the releases of anthrax back in 2001.

8 They were looking for novel strategies to
9 consider, and one of the novel strategies was the
10 pre-placement of life-saving medicines in
11 households to be stored for future use during a
12 declared public health emergency. There are other
13 modalities that have been proposed for bolstering
14 the nation's capacity, and this is just one of
15 those that would be used to respond to large-scale
16 events to get pills closer to people in large
17 quantities and in a rapid manner.

18 So in 2006 -- actually, 2005, CDC was asked
19 to conduct an evaluation study to provide some
20 empirical evidence about the feasibility of placing
21 a cache of antibiotics in individual households and
22 to obtain some baseline data on the behavioral

1 responses of the general public. So we were
2 looking to identify some characteristics of the
3 households and their behavioral responses to having
4 a medkit in their household.

5 So in January of 2006, the Missouri
6 Department of Health and Senior Services agreed to
7 partner with CDC to conduct the evaluation. In
8 collaboration with the Federal Drug
9 Administration [sic], the Centers for Disease
10 Control designed an antibiotic medkit prototype.
11 We wanted to actually develop a prototype and see
12 how we would be able to deliver, or at least
13 package, the doxycycline or other antibiotics, and
14 have it stored properly in the household.

15 So the prototype consisted of a fourfold
16 cardboard blister pack with a five-day supply of
17 medicine. The blister pack was stored in a sealed
18 bag that was transparent on one side and included
19 instructions for use in an open pouch on the
20 outside.

21 The reason for that design is that we wanted
22 the medkit to be stored properly, and we wanted to

1 help resist any temptation to open the medkit. So
2 we made it transparent on one side so the members
3 of the household could actually see what was in the
4 medkit, in that bag; and that we could put the
5 instructions and other fact sheets in the pouch on
6 the outside so that they could pull it out and read
7 it anytime that they felt compelled to get more
8 information.

9 So the medkit prototype, the pack, contained
10 either doxycycline or ciprofloxacin, which are
11 effective countermeasures for anthrax, as you heard
12 Dr. Alexander talk about earlier. Most of the
13 medkit bags distributed contained doxy only. Less
14 than 10 percent of the distributed bags contained
15 both antibiotics.

16 The medkits were produced by IVAX and that's
17 now TEVA Pharmaceuticals. They were shipped to
18 St. Louis and stored in the basement of a local
19 physician's office.

20 For those determined to be medically
21 eligible, all medicines were dispensed under
22 standing orders issued by a physician licensed to

1 practice medicine in the State of Missouri and
2 Illinois. Through a collaborative practice
3 arrangement, six Missouri-licensed, registered
4 nurses actually dispensed the medkits. A medkit
5 bag was Fedex'd to all eligible households.

6 The key evaluation aims were to assess the
7 ability of households to maintain the kit as
8 directed and reserve for future use, to explore
9 other factors that might influence a participant's
10 behavior and acceptability of the medkit, and to
11 finally monitor and assess adverse events
12 associated with the medkit.

13 To meet all federal and state regulatory
14 requirements, the medkit prototype has been
15 evaluated as an investigational new drug. The
16 study protocol was reviewed and approved by three
17 IRBs and the OMB. A local physician was contacted
18 to serve as the medically qualified professional
19 for clinical oversight.

20 Each enrolled household received monetary
21 incentives. At the time of recruitment, when we
22 were trying to recruit them into the study, we gave

1 them a phone card. And when we conducted the
2 baseline interview, they received a \$25 money Visa
3 card. And then at the end of the interview, or at
4 the end of the study and their follow-up interview,
5 they got another \$25 money card.

6 The reason that we provided incentives is,
7 A, to prevent loss to follow-up and, B, our ethics
8 committee ruled that because we were asking them to
9 do something over a period of time and to carry the
10 burden of maintaining this medkit, that it would be
11 appropriate to provide an incentive. And the OMB
12 agreed in their review.

13 The design was prospective over a period of
14 eight months. A baseline interview was conducted
15 in person, and each household member was medically
16 screened. Informed consent was required for each
17 member. The State of Missouri required informed
18 consent for each member of the household. At the
19 time of enrollment, households were randomly
20 assigned to a two-, four-, or eight-month time
21 interval for a follow-up interview and to return
22 their kit.

1 The St. Louis metro area, also a Cities
2 Readiness Initiative participant in the Strategic
3 National Stockpile City Readiness Initiative
4 program, was the pilot test site. Most of the
5 enrolled households were in St. Louis City,
6 St. Louis County, and St. Charles County.

7 The study population consisted of three
8 cohorts. And, by the way, these were considered
9 convenient samples. Some were clients and some
10 were employees of a community health clinic,
11 corporation -- we have 10 corporations; Sigma and
12 AT&T are examples -- and first responders,
13 including the FBI.

14 All data were collected with a PDA and
15 electronically transmitted to a server. We did
16 that so we could reduce the margin for error in
17 data entry.

18 For household enrollment, we had a
19 convenient sample of households, and they were
20 recruited among three cohorts. Final enrollment
21 included 4,250 households with 13,289 household
22 members.

1 The unit for the analytic sample or unit of
2 analysis was the household. One household member
3 was selected as the custodian, and 4.1 percent
4 households, or 174 out of the 4,250, were lost to
5 follow-up. Most of these were because there wasn't
6 anyone home to sign for the FedEx delivery of the
7 medkit, so they didn't get one, and they were
8 dropped out of the study. So our final analytic
9 sample was 4,076 households and about 12,000
10 people.

11 In looking at our household characteristics,
12 about 30 percent of the household respondents in
13 the clinics, the community clinic cohort, had less
14 than a high school education. The annual household
15 income was lowest among the clinic households and
16 most were African-Americans.

17 Almost 60 percent of the clinic households
18 had no health insurance, which makes sense. That's
19 why they were participants in a community health
20 clinic. And 44 percent reported not working
21 outside the home. The household breakdown of
22 children and adults revealed that, within the

1 clinic cohort, there was a greater proportion of
2 children than in the other two cohort households.

3 In looking at our behavioral outcomes,
4 97 percent of all study respondents, meaning the
5 household, return the household medkits upon
6 completion of the study. And there was no
7 statistical significant difference between the
8 cohorts for returning. One-hundred and thirty
9 households did not return their medkits, 125 of
10 these households cannot locate their medkit, and
11 five simply refused to return them.

12 Four households reported having used their
13 medkit. All four were in the clinic cohort. One
14 household was an elderly woman who used her medkit
15 during a declared emergency for winter storm. The
16 governor of Missouri declared an emergency during
17 the time of the study for a really bad winter
18 storm, a blizzard, and she did not understand the
19 nuances of the emergency and used her medkit. Two
20 household members said they used it for a sore
21 throat, two households. And one refused to state
22 why the pills were taken.

1 Among those medkit bags that were returned,
2 all but 34 were intact and no pills were missing
3 from those that had been opened. Curiosity about
4 the contents was the most frequently mentioned
5 reason for opening the medkit bag. And most of
6 those that did open the bag were from the clinic
7 cohort.

8 We also assessed antibiotic knowledge; in
9 other words, when is it appropriate to take
10 antibiotics. It is important to note that almost
11 60 percent of the clinic household respondents
12 reported that antibiotics were good for a cold.
13 And the way that we assessed this was, we said
14 we're going to read a few statements regarding
15 antibiotics. Please tell me if you think the
16 statement is true or false: A, antibiotics kill
17 bacteria, but never kill viruses; when you have a
18 cold, antibiotics can be used to prevent you from
19 becoming more sick; or C, you can stop taking
20 antibiotics as soon as you feel better.

21 In assessing the social factors, at the time
22 of the follow-up interview, more than 75 percent

1 reported that having the emergency medkit in their
2 home increased their awareness of the need to
3 prepare for a public health emergency, including a
4 terrorist attack. Overall, 75 percent of all
5 respondents reported that they feel not too
6 prepared or not at all prepared for such an attack.
7 In other words, having the medkit made them think
8 about getting more prepared.

9 The majority of the study participants,
10 94 percent or more in each cohort, reported that
11 based on their experience with the study, they
12 would like to have a medkit in their home. The
13 majority of respondents also said that they would
14 pay for a medkit. The average price that
15 households would pay per person was \$23.

16 So, in conclusion, a majority of the
17 households appropriately followed the instructions
18 regarding storage and reserving the medkit for use
19 until directed by public officials. A large
20 proportion of the households reported that they
21 would be willing to have emergency medkits in their
22 home, and they would be willing to purchase these

1 medkits.

2 So the overarching aim of the medkit project
3 was met, which was to evaluate a strategy that
4 addresses the timeliness of distributing
5 antibiotics to the general public by letting them
6 maintain the antibiotics in their household. And
7 while the medkit project demonstrated success for
8 stockpiling antibiotics in households, I think it's
9 important to note a couple of important limitations
10 that should be considered in the context of this
11 study.

12 While we firmly believe that we have
13 internal validity for this study, we feel that we
14 have very limited external validity. And by that I
15 mean generalizability to other populations. This
16 was a convenient sample in a metro area, three
17 different counties. And in no way, shape, or form
18 can that be generalizable to a U.S. population.

19 The other caution is that we really could
20 not assess the magnitude of potential bias that
21 providing the incentives may have had on the
22 household motivation to return the medkit.

1 So with that said, pending any questions,
2 that concludes my presentation.

3 **Questions and Clarifications**

4 DR. MOORE: Thank you, Dr. Neff.

5 We have a few minutes for questions and
6 clarifications of the first three speakers. I'll
7 start off.

8 Dr. Neff, can you hear me?

9 DR. NEFF: Yes, I can you hear you.

10 DR. MOORE: This is Dr. Moore. A question
11 about the antibiotic knowledge slide. Was there
12 any attempt to educate the recipients of the medkit
13 between the baseline and the follow-up? That is,
14 educate them about the role of antibiotics and the
15 importance of their lack of effect against viruses?

16 DR. NEFF: No. We did not do that --

17 DR. MOORE: Thank you.

18 DR. NEFF: -- because we actually wanted to
19 evaluate their knowledge without -- you know, we
20 didn't want to bias the evaluation. We wanted to
21 actually see -- we wanted to actually assess what
22 they would say antibiotics could be used for. And

1 the 60 percent is actually in alignment with other
2 national studies about antibiotic knowledge.

3 DR. MOORE: Thank you for that
4 clarification. Yes, that's not surprising to me,
5 those results. Thank you for that clarification.

6 Next, we'll go to,
7 actually -- Dr. Reidenberg?

8 DR. REIDENBERG: Dr. Reidenberg for
9 Dr. Neff. Two questions. Confirm again that the
10 total duration of follow-up was eight months. And
11 I want to know whether those eight months included
12 the summer and autumn.

13 DR. NEFF: Yes. It was eight months. And,
14 yes, it did. It did include the summer and autumn.

15 DR. REIDENBERG: Thank you.

16 DR. MOORE: Dr. Vaida, you had a question?

17 DR. VAIDA: Yes. Did the participants know
18 that there was going to be another \$25 incentive at
19 the end of the study?

20 DR. NEFF: No, they did not. We did not
21 tell them that.

22 DR. MOORE: If there are no other questions,

1 then we will proceed to the next presentation.

2 Dr. Lynfield from the Minnesota Department
3 of Health.

4 Oh, I'm sorry. I've overlooked somebody
5 with a question. I apologize.

6 Ms. Morrato, go ahead.

7 DR. MORRATO: Are we allowed to ask
8 questions to Dr. Alexander and Ms. Cohen? It's for
9 all presenters?

10 DR. MOORE: Yes, yes.

11 DR. MORRATO: I had a question with regard
12 to the study populations for consumer testing. I
13 know for general over-the-counter medicines, it's a
14 general population of ordinary individuals. But
15 one of the proposals today is to actually look at
16 emergency first responders. So is there a
17 consideration as to the population? Could future
18 testing just be targeted at emergency responder
19 type individuals? Or do you still need to go more
20 broadly to the general population?

21 It relates to the literacy goals and
22 measures on percent who understand, et cetera.

1 MS. COHEN: Again, I really think that
2 depends on what we're looking to accomplish and
3 what the overall target population would be. So
4 you could do a study with just emergency responders
5 if we think that that's who ultimately going to get
6 it and nobody else.

7 I think that if we think that the general
8 public will be getting it at some point, I think
9 that it might be prudent to test it with them,
10 again, if we do think that they're going to get it
11 at some point down the line.

12 Does that answer your question?

13 DR. MORRATO: Yes. I was just thinking of
14 it in a narrow prescription drug-indicated use.

15 MS. COHEN: Right.

16 DR. MORRATO: You would go for the
17 population that it's indicated in versus worrying
18 about all off-label users.

19 MS. COHEN: Right.

20 DR. MORRATO: And then you mentioned -- I
21 understand that the percent that is -- the
22 threshold for success -- I think is how you called

1 it -- is drug specific. But can you give us a
2 sense of the ranges that you've used for other
3 products, so we get an idea of general
4 acceptability?

5 DR. LEONARD-SEGAL: Andrea Leonard-Segal
6 here. The target threshold for success is a very
7 complicated number to come up with. And we have
8 done different kinds of numbers for different kinds
9 of studies. We're talking about label
10 comprehension studies, self-selection studies,
11 actual-use studies, maybe human factor studies.
12 We've used different targets, depending on the
13 magnitude of the importance of the success element
14 that we are studying.

15 In a label comprehension study, you could
16 have different key factors for success or different
17 key elements that are important to understand. If
18 we thought that one was less important than the
19 other, then we would come up with a different
20 target.

21 So I would say that -- and also remembering
22 that label comprehension studies are not the key

1 study here. The key study is the use study. We
2 would have probably different targets for the label
3 comp on elements compared to maybe a particular
4 actual use element for this.

5 I would say that in general, we have
6 accepted different kinds of comprehension rates
7 depending on the population for different elements,
8 as low as maybe 70 percent, as high as -- there was
9 one study that we did on -- that a couple of people
10 in this room will remember, probably. Well, maybe
11 not. I'm not sure this one ever got presented to
12 the AC.

13 But it was for the orlistat weight loss
14 drug, where we looked at self-selection rates in
15 people that were cyclosporine users because that is
16 a complete contraindication to the use of orlistat,
17 because orlistat interferes with the absorption of
18 the cyclosporine. The target success rate on
19 self-selection for that study was 100 percent.
20 That may be the only time we've gone that high, but
21 we have to look at the magnitude of the issue.
22 Could be anything.

1 DR. MOORE: Thank you.

2 Let's move on now to -- oh, I'm sorry.

3 Sorry, Dr. Parker, go ahead.

4 DR. PARKER: Ruth Parker. One other
5 question. This is for Dr. Neff. Just looking at
6 the behavioral outcomes, I just wanted to see if by
7 chance you have any further data at all specific to
8 the clinic population, since that's the only
9 population that more closely reflects the reality
10 that about 30 percent or so of adults in our
11 country haven't graduated from high school. And
12 that's the only population that comes close to
13 reflecting that.

14 I wondered if you have any more information
15 about the did-not-return, the 92 of that cohort out
16 of a total population that you're calling 1443. It
17 says that one refused and 91 were unable to locate
18 the kit.

19 What more do you know about that number?

20 DR. NEFF: Actually, we did not follow up or
21 do any kind of qualitative assessment to get a
22 better understanding of why they couldn't locate

1 the kit. So we don't really have any additional
2 information other than they could not locate it or
3 return it.

4 DR. MOORE: I hope I didn't overlook anybody
5 else's questions? No? All right.

6 With that, Dr. Lynfield, Minnesota
7 Department of Health.

8 **Presentation - Ruth Lynfield**

9 DR. LYNFIELD: Good morning. Thank you for
10 the opportunity to speak about the Minnesota
11 experience with home antibiotic kits in postal
12 workers participating in antibiotic delivery
13 activities.

14 The Minnesota Department of Health, or MDH,
15 partnered with HHS and the U.S. Postal Service on a
16 project initially through the Cities Readiness
17 Initiative, now referred to as the National Postal
18 Model. In this plan, voluntary male carriers
19 accompanied by peace officers would deliver
20 doxycycline, one bottle of 20 tablets, to
21 residencies in predetermined ZIP codes of the
22 Minneapolis-St. Paul area following an anthrax

1 event. The area covered contains approximately
2 205,000 households.

3 Under an FDA emergency-use authorization,
4 the participating letter carriers and their
5 household members are provided with a household
6 antibiotic kit, and the participants have an
7 individual antibiotic kit that is kept at the
8 workplace. The unions, representing the U.S.
9 Postal Service carriers, had a provision for
10 screening and providing an N-95 respirator for each
11 participant in addition to the antibiotic kits.

12 Participants were solicited by the U.S.
13 Postal Service management and union
14 representatives, and screening in Minnesota began
15 in spring 2009. This included the Federal
16 Occupational Health, also known as FOH, N-95
17 screening form, fit testing. And NDH provided
18 doxycycline screening for participants and
19 household members.

20 There were 386 eligible letter carriers in
21 the fall of 2009. These individuals received a
22 home antibiotic kit and an individual antibiotic

1 kit in the fall of 2009. Again, the home
2 antibiotic kit contained one bottle of 20 tablets
3 of doxycycline per participant and per household
4 member. The individual antibiotic kit contained
5 one bottle per participating letter carrier that
6 was stored at the workplace.

7 The requirement in fall 2009 included a
8 semi-annual health and kit status update and yearly
9 collection and replacement of the home antibiotic
10 kits and individual antibiotic kits. MDH, in
11 cooperation with the U.S. Postal Service and HHS,
12 developed a knowledge survey that was included in
13 the six-month status update mailing in spring 2010
14 for the first group of participants. The survey
15 included questions on their understanding of
16 anthrax, antibiotics, and the household antibiotic
17 kit.

18 The response rate was 57 percent. The
19 demographics include the following. 90 percent
20 were white, 71 percent were male, 74 percent had at
21 least some college education, and 50 percent had
22 children less than or equal to 18 years of age.

1 Ninety-one percent understood that anthrax
2 is a fatal disease if not treated and 63 percent
3 knew that anthrax was not a contagious disease.
4 Ninety-seven percent knew that the home antibiotic
5 kit should be used only when informed by public
6 health officials. Eighty-five percent had no
7 concerns keeping antibiotics at home, and 6 percent
8 were concerned about the yearly collection of the
9 home antibiotic kit.

10 When asked about the antibiotics required
11 for anthrax prophylaxis, only one-third knew that
12 60 days of prophylaxis would be required.
13 Forty-four percent thought that 10 days would be
14 enough, and 22 percent did not know. Sixty-one
15 percent incorrectly thought that the home
16 antibiotic kit was sufficient to provide all the
17 antibiotic protection for that household.

18 Of those who knew additional antibiotics
19 would be needed for their household, 51 percent
20 indicated that remaining antibiotics would be
21 obtained at a public health clinic, and 18 percent
22 thought that antibiotics would be delivered as part

1 of the postal plan to their homes, and that the one
2 bottle delivered per residence would provide enough
3 protection.

4 I do want to just say that as part of the
5 process of recruiting these participants, there was
6 some information shared about anthrax. And
7 therefore, they did have information provided at
8 the beginning of this that may have enabled them to
9 answer the questions.

10 At the first home antibiotic kit status
11 check, 9 of 386 opted out or retired and returned
12 the kits; 365 out of 377 returned the status
13 update. Some status updates were not returned at
14 the six-month mark, but were returned as late as
15 the one-year mark. All of these individuals,
16 however, reported that the medkits had not been
17 opened.

18 Three hundred sixty-seven home antibiotic
19 kits were collected and replaced at one year, and
20 of those, none have been opened. Ten were not
21 returned. Five continued to be active volunteers,
22 and they did have replacement of their medkit.

1 Three were deactivated. One had transferred
2 location and took the kit. And one opted out and
3 reported that the kit was missing.

4 Ongoing status checks were as follows.
5 Between October 2010 and March 2011, there were
6 327 participants. Ninety-five percent turned in
7 the six-month form, 286 returned on time. Another
8 24 returned several months later after repeated
9 mailings.

10 All 310 knew where their medkit was and that
11 it was unopened. Ninety-one percent indicated that
12 they did not have a change in health status or
13 composition of the household.

14 Between April 2011 and October 2011, there
15 were 337 participants. These responses were sent
16 to HHS because activities related to health safety
17 began to be transitioned to HHS in December 2010
18 because of increasing resources required to do this
19 and decreasing resources at the Minnesota
20 Department of Health, so that there was an overall
21 responsibility-shifting as of October 2011 EUA.

22 Ninety-nine percent turned in a completed

1 six-month form; 268 returned on time; another 66
2 returned after the deadline. Ninety-seven percent
3 knew where their medkit was and that it was
4 unopened, and 87 percent had no change in health
5 status or composition of household.

6 It is very labor intensive to collect these
7 kits because the kit needs to be opened, paper
8 removed and recycled. Labels need to be removed
9 from each bottle and shredded because they contain
10 personal identifiers. And the drug needs to be
11 shipped for disposal.

12 In summary, for the most part, the household
13 antibiotic kits were able to be stored in the home
14 and turned in at the one-year mark in this group of
15 several hundred volunteers. There was not much
16 change that occurred in household composition. The
17 knowledge survey from 2010 found that there were
18 some misunderstandings about anthrax post-exposure
19 prophylaxis.

20 Some issues and challenges include that the
21 drug fact sheets in the medkits are lengthy, of a
22 high reading level, and not translated into other

1 languages. The annual renewal was very resource
2 intensive at the local level due to the medkit
3 collection and replacement.

4 In fall 2011, the EUA was amended so that we
5 were able to use the original manufacturing
6 container and, therefore, the expiration date
7 rather than do annual replacement.

8 Some things to be aware of is that a
9 bioterrorism strain may not be antibiotic
10 resistant. We do need additional data on the use
11 of medkits because the Minnesota postal participant
12 data may not be generalizable to other areas and to
13 other groups. And there were concerns raised by
14 participants for the availability of other
15 antibiotics for people who can't take doxycycline.

16 We also need to address ready access for
17 post-exposure antibiotics for accompanying law
18 enforcement and other first responders. However,
19 for a large-scale medkit approach, there are
20 tremendous sustainability and feasibility
21 challenges, which include the following.

22 The collection and replacement of medkits

1 are labor intensive. Disposal of large amounts of
2 unused antibiotics are expensive and may have
3 environmental impact. And there may be concern, as
4 discussed earlier, about the unintended adverse
5 consequences, such as using the doxycycline for
6 other purposes.

7 We suggest that it would be useful to
8 evaluate the medkits with other groups and areas
9 and also to consider other options for post-
10 exposure antibiotic access. It is important to
11 forward position antibiotics for first responders.
12 However, there are other possibilities that we're
13 evaluating in addition to storage at home. And
14 this may include the evaluating the ability to
15 store and rapidly access and dispense antibiotic
16 prophylaxis at the workplace and other central
17 locations for first responders and families so that
18 the kits could be stored at a workplace, include
19 antibiotics for the families. This would allow
20 enhanced security of the drug. People would know
21 where the drugs are. If there's turnover in
22 personnel, you don't need to track down the home

1 antibiotic kits. You can keep up with who needs an
2 antibiotic kit. It also is worth considering, for
3 certain high-risk first responders, pre-exposure
4 anthrax vaccine.

5 Clearly, they may not be able to have a one-
6 size-fits-all approach for responders and that the
7 risks and benefits of possible approaches should be
8 weighed. It is important, however, to evaluate the
9 understanding of responders regarding anthrax and
10 regarding post-exposure prophylaxis. The
11 educational materials that are provided to first
12 responders about the use of antibiotics may need to
13 be adjusted and may need to be provided multiple
14 times. It may be useful also to have materials
15 that are easy to access and to provide refresher
16 training.

17 Finally, I would like to thank the many
18 individuals who helped us in Minneapolis and
19 St. Paul.

20 DR. MOORE: Thank you very much,
21 Dr. Lynfield.

22 Let's move on now to Susan Collier-Monarez,

1 who will be representing -- from the Department of
2 Homeland Security. I hope I said your last name
3 right.

4 **Presentation - Susan Collier-Monarez**

5 DR. COLLIER-MONAREZ: Good morning. I
6 appreciate the opportunity to come and give a
7 perspective from Homeland Security on the ongoing
8 concerns or threats that biological agents and
9 Bacillus anthracis, the causative agent of anthrax,
10 present. I will just get started.

11 In 2008, the WMD commission, a
12 Congressional-mandated commission, did an
13 analysis on the preparedness posture of the United
14 States for WMD. In their evaluation, they
15 concluded that, more likely than not, there would
16 be an attack using a WMD somewhere in the world by
17 2013.

18 Part of their evaluation also looked at the
19 potential for using -- among the traditional WMD
20 agents, chemical, biological radiological, or
21 nuclear, the relative potential of using one of the
22 agents. And their conclusion was that the use of a

1 biological agent was more likely due to the ability
2 of an adversary to acquire and produce biological
3 agents over the nuclear threat potential.

4 In fact, what we see is that historically,
5 of the biological agents, *Bacillus anthracis*,
6 anthrax, has been identified by adversaries as
7 something of interest, an agent of interest. As
8 recently as 2003 in Afghanistan, there were
9 materials found in the training camps of Al-Qa'ida
10 that indicated that there was an interest in
11 acquiring and using biological and chemical agents,
12 including *Bacillus anthracis*.

13 In 2001, I think we're all familiar with the
14 Amerithrax event. Anthrax was put in the mail and
15 distributed through the postal system. And it
16 caused 22 infections and 5 deaths, and resulted in
17 more than a billion dollars in economic damage.

18 Perhaps most alarming was actually what
19 happened in 1993. The Japanese cult Aum Shinrikyo
20 actually managed to acquire, produce, and
21 disseminate, in a mechanism that would have caused
22 significant mass casualties, *Bacillus anthracis*.

1 They produced it and disseminated it from both
2 rooftop sprayers as well as a moving vehicle. It
3 was only because of an oversight on their part,
4 that they had actually acquired an avirulent
5 strain, that the outcome of that particular event
6 wasn't more catastrophic to the population that was
7 targeted.

8 The government has put into place robust
9 biosecurity and biosafety measures to reduce, to
10 eliminate, the potential for acquisition of
11 biological agents within public health or
12 biodefense research labs. However, *Bacillus*
13 *anthracis*, much like many of the other biological
14 agents, occurs naturally in many countries. In
15 2012 alone, there have been at least three reported
16 outbreaks in sub-Saharan Africa. And as you can
17 see by this slide, the global distribution of
18 *Bacillus anthracis* is in places where there are
19 individuals or groups of individuals who have
20 demonstrated the intent or the motivation to do
21 harm to the United States or Western allies. And
22 so despite robust biosecurity and biosafety

1 measures being put in place, there is always the
2 opportunity for an adversary to acquire the agent
3 from the environment.

4 Biological agents are unique in that they
5 are able to be acquired/produced in a way that
6 United States government -- despite robust
7 processes and procedures in place to enhance our
8 ability to interdict or detect, it may be
9 impossible for us to be aware of an adversary
10 producing biological agents.

11 The footprint of biological agent production
12 can be relatively small. I mean, essentially, to
13 produce the agent really requires only a small
14 footprint of the ability to maintain amenable
15 temperatures and acquired growth medium, and can be
16 done in something as small as a garage, which would
17 be under the radar or even the most robust
18 surveillance program.

19 Past experience back in 2001 with the
20 Amerithrax events, there were 5 deaths and 22
21 illnesses, and 30,000 people who received
22 antibiotic treatment. The economic cost was

1 greater than a billion dollars. And by many
2 standards, this was a limited attack.

3 Should the attack be more widely
4 disseminated, the potential exposure numbers could
5 be up to 3 million people. And given just the
6 pathogenecity associated with *Bacillus anthracis*,
7 the illnesses could reach almost 500,000 with the
8 number of deaths close to that without interdictive
9 measures. And then economic cost could be
10 certainly within the trillions.

11 This last slide that I want to leave you
12 with is something that we consider very intensely
13 when looking at preparedness and planning efforts
14 within Homeland Security, and I know within HHS as
15 well, is that the response time following an event
16 is absolutely critical.

17 This is a purely notional graph, but what I
18 think it gives you is a sense of what has to occur
19 following the release of *Bacillus anthracis* to
20 ensure that we have the most meaningful public
21 health response and the ability to mitigate illness
22 to the extent possible.

1 So what you see on the X axis, the timeline,
2 is that each step following the release of an
3 organism, the detect, the time to detect, has
4 intrinsic times associated with it. Whether it's
5 via environmental detection or through robust
6 public health surveillance, there's a decision
7 period when we know that this has moved from one or
8 two cases that could be anomalies to something
9 that's more widespread and systematic. There are
10 procedures in place now to have rapid distribution
11 of post-exposure antibiotics. And then the time to
12 dispense is certainly critical beyond that.

13 So what you get, when you add up all of the
14 time associated with one of these points following
15 an event, is that it becomes very clear that if
16 there is a delay in any one of these aspects -- and
17 as I had mentioned a few slides ago, the production
18 and dissemination of a biological agent may not be
19 something that the government, despite its best
20 efforts, is fully prepared to intervene or mitigate
21 in the early stages -- what we're looking at is the
22 percentage of an ill population that rapidly moves

1 from ill to potentially mortally ill or dead,
2 depending on the delays associated with the
3 distribution of antibiotics.

4 So what we know is that there is the
5 potential for an adversary to acquire and use a
6 biological agent, specifically *Bacillus anthracis*,
7 and that if they do so, it is absolutely critical
8 that we have the measures in place to be able to
9 mitigate and reduce the health effects associated
10 with that to the extent possible.

11 DR. MOORE: Thank you.

12 We'll now move to the sponsors'
13 presentations. I'll have to read this disclaimer.

14 Both the Food and Drug Administration, the
15 FDA, and the public believe in a transparent
16 process for information gathering and decision
17 making. To ensure such transparency at the
18 advisory committee meeting, the FDA believes that
19 it is important to understand the context of an
20 individual's presentation.

21 For this reason, the FDA encourages all
22 participants, including the sponsor's non-employee

1 presenters, to advise the committee of any
2 financial relationships that they may have with the
3 firm at issue, such as consulting fees, travel
4 expenses, honoraria, and interests in the sponsor,
5 including equity interests and those based upon the
6 outcome of the meeting.

7 Likewise, the FDA encourages you at the
8 beginning of your presentation to advise the
9 committee if you do not have any such financial
10 relationships. If you choose not to address this
11 issue of financial relationships at the beginning
12 of your presentation, it will not preclude you from
13 speaking.

14 We're going to move now to Dr. Korch.

15 DR. KORCH: No relationships to any
16 organization, no financial interests.

17 DR. MOORE: Thank you.

18 **Sponsor Presentation - George Korch**

19 DR. KORCH: Thank you very much for the
20 opportunity here to address the combined advisory
21 committees on the effort that's under
22 consideration. I also want to thank Dr. Deb Yeskey

1 and Ms. Helen Stallings for all of their hard work
2 in getting us to this point, as well as to our
3 other colleagues at HHS and elsewhere, our FDA
4 colleagues as well across multiple offices, and for
5 the opportunity here to have you all assist us in
6 terms of evaluating the public health implications
7 of medkits, bacterial resistance, et cetera,
8 benefits and risks for the individual, about other
9 additional studies, recommended studies, and the
10 design of those studies, to properly evaluate the
11 proposed methodologies, and then finally about
12 additional recommended studies on such issues as
13 formulation for semi-solid dosing for pediatric
14 populations and dysphagic adults.

15 The entire effort really is all about our
16 nation's commitment to being sure that we can
17 minimize, to the greatest extent possible, the loss
18 of life and the impact on our healthcare systems
19 from what would be a major public health event, a
20 crisis, to experience an attack from anthrax. And
21 while this is thought to be a low-frequency event,
22 it would have very high consequences, as described

1 just a moment ago by Dr. Collier-Monarez. And it's
2 received serious attention, as it should, in our
3 planning, and yet there is more that we can do.

4 We want to be able to improve our national
5 preparedness for anthrax attack by ensuring, in
6 this particular instance, that our first responders
7 have immediate access to the medicines that they
8 would need in the case of an attack. And with such
9 preparation, our first responders would be
10 available to assist the rest of the community. We
11 also want the first responders to have peace of
12 mind from knowing that they and other members of
13 their households would have prophylactic
14 antibiotics immediately available in the event of
15 bioterrorism affecting the community.

16 I want to stress at this time that this is
17 not a specific government endorsement aimed at the
18 exclusive needs of this particular community, but
19 it is a fairly well-delineated group of individuals
20 in the community who would serve as our first steps
21 in demonstrating the feasibility of a probable
22 better or larger medkit option. And we want first

1 responders to be prepared to have access to those
2 particular capabilities.

3 We have a range of policies, investments,
4 and plans derived from the overarching federal,
5 state, local, and tribal commitments to prepare,
6 and respond, and recover from a wide variety of
7 threats. The Public Health Emergency Medical
8 Countermeasure Enterprise, or PHEMCE, is a federal
9 interagency partnership that I'll describe
10 momentarily. The mission of the PHEMCE is to
11 develop and sustain the capability to respond to a
12 wide variety of public health emergencies, as well
13 as being good stewards and resources of the
14 materials being made to do so.

15 Now, anthrax has rightfully occupied a great
16 deal of attention as a major threat. Preparedness,
17 as it relates to antibiotics, for anthrax is the
18 focus of a number of strategic directives and
19 initiatives such as the presidential policy
20 directive Number 8 on national preparedness.

21 This directive includes language that
22 directs federal authorities to develop national

1 guidance for public-private coordination of
2 prepositioning, distribution, and dispensing of
3 medical countermeasures. It also directs the
4 authorities to integrate ethical principles and
5 public engagement in these efforts, along with the
6 overall context of public health planning for
7 bioterrorism response, and to give priority to
8 improve the dispensing capabilities, and for
9 developing prepositioning strategies.

10 I will also discuss the establishment of a
11 capability -- and you've already heard that from
12 the U.S. Postal Service model -- as a delivery
13 mechanism for antibiotics; home medkits as a
14 concept, as you've heard already in place and the
15 program set up under this postal service model. I
16 will also touch briefly on Presidential Order 13527
17 to establish federal capability for the timely
18 provision of medical countermeasures following a
19 biological attack, and data gathered from this
20 program are already providing us with important
21 information on proper retention of these kits in
22 the home.

1 This quickly is the responsibility and the
2 structure of the PHEMCE. As I mentioned, it's a
3 coordinating interagency effort that begun around
4 2006 or 2007, responsible for the finding and
5 prioritizing requirements for medical
6 countermeasures for chemical, biological,
7 radiological, nuclear threats as well as emerging
8 infectious diseases and pandemic diseases.

9 It focuses on the full life cycle here,
10 research, development, procurement activities,
11 establishing and deploying deployment and use
12 strategies. It's led by the Assistant Secretary
13 for Preparedness Response and includes, as well as
14 ASPR and BARDA, the other three primary HHS
15 operational divisions, CDC, FDA, and NIH.

16 It takes a comprehensive end-end approach to
17 plans that consider multiple aspects of medical
18 countermeasure mission, including, as you see, the
19 feedback mechanisms that run around the perimeter
20 of this particular linear sequence, to include the
21 needs of stakeholders and communities in
22 consideration of our needs. You'll also notice

1 that the FDA is a constituent of this, relevant to
2 all the issues, all across this value chain, this
3 linear process, for product development and use.

4 The PHEMCE has the ability, through the
5 Office of the Assistant Secretary and the Office of
6 the Secretary, to engage the National Biodefense
7 Science Board, which is a senior-level FACA
8 advisory committee from outside government.

9 Now, I mentioned that the U.S. has invested
10 a good deal of time, money, and energy into
11 materials and strategies to mitigate against such
12 an event. What we have in terms of anthrax is a
13 layered response. Consider this a preparation in
14 depth.

15 We have in place a system of early detectors
16 and medical surveillance systems whose aim is to
17 notify public health, medical, and security
18 individuals as soon as possible that we have had an
19 exposure to aerosolized anthrax. And Susan
20 Coller-Monarez provided in that graphic a display
21 of the timeline given to us following an event.

22 Now, we assess from computer simulations and

1 from response modeling time that it's of essence to
2 recognize and respond to such events as quickly as
3 possible, because as the hours tick by from the
4 first recognition of such event, we risk losing
5 hundreds of thousands of lives.

6 The current strategy is to provide
7 antibiotics, either ciprofloxacin or doxycycline,
8 for all individuals in the affected area,
9 ultimately with a 60-day supply of antibiotics.
10 And this process would be provided, as described,
11 as an initial 10-day supply for the acute phase of
12 the response and then a second administration of
13 50 days of drug.

14 We know that antibiotics and vaccines are
15 very effective in preventing the advent of a large
16 number of sick and dying individuals and that the
17 systems put into place by the federal government,
18 by other communities, and commercial organizations,
19 to essentially stockpile antibiotics is critical to
20 an effective response. Yet, we understand that
21 even with these systems, there are created
22 difficulties and vulnerabilities. And in the big

1 picture, what we are really discussing today, this
2 medkit for our first responder communities, is only
3 a little sliver of the anthrax strategy during the
4 acute initial phases of this response. But every
5 increment in planning helps to add to a more robust
6 and resilient system.

7 What we have accomplished over the last
8 decade or so is the following. We now have a
9 stockpile of approved antibiotics that we feel
10 would be able to handle several large simultaneous
11 events.

12 We are in the process of evaluating other
13 antimicrobials to extend our capability for
14 response. We've examined a variety of other
15 distribution methods to provide these important
16 prophylaxes to the population in need. We have
17 invested in several different antitoxins to aid in
18 the treatment of disease. And we have stockpiled,
19 and coordinated, and continued to invest in
20 vaccines, both current technologies and in future
21 candidates, principally for use in post-exposure
22 scenarios and in conjunction with our intended use

1 of the antibiotics to further strengthen our
2 ability to function well, even after the initial
3 event, and to ensure our populations that they can
4 remain safely protected in these affected
5 localities.

6 The Obama administration has built upon the
7 earlier efforts of the prior administration to put
8 more emphasis on being sure that plans and policies
9 were in place or are in place for the specific
10 activities necessary to respond to an anthrax
11 event. This emergency or, I'm sorry, this
12 executive order, shown here, calls for a rapid
13 federal response to supplement state, local, and
14 territorial efforts. And the EO also calls out
15 specifically that there should be formally
16 established, at the national U.S. Postal Service, a
17 delivery model for antimicrobials for this initial
18 response at the community level, as well as
19 requiring that the federal government work to
20 further these strategies for supplementing state
21 and local jurisdiction capabilities for
22 distribution and dispensing plans. And medkits

1 could be considered a component for ensuring the
2 readiness of federal and mission-essential first
3 responders in section number 4.

4 I mentioned also that the U.S. government is
5 pursuing a preparation in-depth strategy to prepare
6 and respond to an anthrax attack. And this is a
7 quick list of the current and potential mechanisms
8 to provide for community-level antibiotics.

9 As mentioned before, our primary strategy is
10 the centrally-managed materials held in the federal
11 strategic national stockpile that would be deployed
12 to localities through open points of distribution,
13 or PODS. There are localities that have been
14 established locally for procured caches for
15 specific use, as was mentioned slightly earlier.
16 And there are workplace, or closed PODs, or caches
17 as well, including those held by some federal
18 agencies. And there's also a limited U.S. Postal
19 Service model that was just described, which is
20 beginning to expand -- and I'll describe that a
21 little bit more -- from the first -- that's called
22 test-bed site -- as a component. And home medkits

1 have been associated with this particular model.

2 Other modalities that we're considering for
3 distribution would entail the availability of
4 medkits for more widespread predeployment. And the
5 two potential strategies possible and described
6 here would be one limited application of medkits
7 and then finally a much broader application. But
8 again, I stress the primary strategy at this point
9 is through use of the central management and POD
10 distribution.

11 The Project Bioshield amended the Federal
12 Drug and Cosmetic Act to allow the issuance of
13 emergency-use authorization during the initial or
14 acute phase of a domestic emergency. And the EUAs,
15 as you've heard, allow for the use of products that
16 were otherwise unapproved, or not approved for the
17 intended use.

18 The postal EUA includes the following
19 information in the executive summary: a
20 description of a product and its intended use; the
21 rationale behind the use of the products under the
22 EUA; identification, explanation of the unmet need;

1 description of the product's approval or clearance
2 status; identification of any approved alternate
3 product's safety and efficacy information, risks,
4 et cetera.

5 The FDA commissioner established additional
6 considerations and conditions of authorization to
7 include, for the postal model, home kits and the
8 individual kit status reporting, as you heard
9 Dr. Lynfield describe; reporting on municipalities;
10 medical screening by potential U.S. Postal Service
11 participants and their immediate household members;
12 and the requirement to provide fact sheets and
13 forms to participating municipalities; and
14 responsibility for doxycycline, procurement; drug
15 accountability; inventory records; and adverse
16 event reporting.

17 The program itself initially started in
18 Minneapolis. It has just been made operational.
19 It is expanding to Louisville, Kentucky and San
20 Diego, California. And to join will be
21 Philadelphia, Pennsylvania, and Boston,
22 Massachusetts.

1 Preparing the nation for an anthrax attack
2 has been a priority of the PHEMCE since its
3 inception as well, and the concept of the whole
4 medical kit has been around in concept since about
5 July of 2005. The initial investment in the
6 concept and discussion with the FDA regarding how
7 one might go about establishing such a capability
8 led the CDC to filing an IND for the 10-day course
9 of treatment for family members and for the
10 clinical study that you heard described, conducted
11 to determine whether the kits would be properly
12 maintained and returned intact.

13 The results of the study were encouraging,
14 as also described by Dr. Neff, with 97 percent of
15 the kits returned intact. FDA provided further
16 information regarding the necessary components to
17 file as an NDA. And the U.S. public postal service
18 model and the issuance of the EUA for home medkits,
19 allowing for distribution of these kits to postal
20 workers, was again a milestone in the general
21 concept of the use of such kits. The EUA has been
22 renewed every year since 2008.

1 The push for the general medkit was put on
2 hiatus for a while due to concerns about potential
3 misuse, the issue of adverse effects, a
4 contribution towards community-level antibiotic
5 resistance. And studies funded by BARDA, that I'll
6 describe in a moment, went forward on issues of
7 palatability and label comprehension.

8 However, we've resurrected this concept in
9 response to both the December 2009 executive order
10 and as a function of a series of tabletop exercises
11 at national level, suggesting that distribution of
12 medical countermeasures during the critical initial
13 stages could be significantly benefitted with
14 additional mechanisms to disperse these
15 antibiotics.

16 In January 2011, we received the study
17 report on palatability. And in July of last year,
18 the FDA, under CDC request, issued an EUA for mass
19 dispensing of doxycycline because of the need for
20 storage and distribution of oral antibiotics by
21 stakeholders for preparedness purposes in advance
22 of an actual anthrax event, with the intent that

1 they may be dispensed post-event as part of a mass
2 distribution strategy.

3 Now, stakeholders means here public
4 agencies, or its delegate, that has legal
5 responsibility and authority for responding to an
6 incident, based on a political or geographical
7 boundary. And we at ASPR also requested that the
8 IOM take a look at the concept of far-forward
9 deployment of medical countermeasures. And we also
10 held stakeholder outreach and public surveys for
11 this concept, most recently in Seattle, King
12 County. ASPR then decided to pursue establishing
13 of this capability, as sponsor, with the filing of
14 BARDA of an IND for the medkit.

15 Regarding the issues of home positioning and
16 antibiotics, the FDA earlier provided an official
17 guidance to BARDA and to ASPR as a suggested path
18 forward for the kits, requesting studies that I'll
19 describe in a moment be performed on issues related
20 to dosing of all members of the family, and
21 especially aimed at pediatric and dysphagic adults,
22 since this at this point in time is proposed as

1 only a single formulation of 100-milligram tablets
2 of doxycycline provided per each family member.

3 So let me review quickly the results of some
4 of these studies. Regarding the palatability study
5 performed as a non-IND study, under an IRB approved
6 by Northland Labs in Chicago, Illinois, the
7 objective of this study is the identification of
8 foodstuffs that will most successfully mask the
9 rather unpleasant taste of doxycycline, oral-dosage
10 forms, intended to be used in the pediatric and
11 dysphagic elderly populations during an anthrax
12 attack or other national, biological emergency.

13 Sixty-one panelists were asked to taste and
14 grade 16 different foodstuffs and pharmaceutical
15 flavorings, tasting up to four different products
16 per sitting. And shown here were the items that
17 scored highest, and the qualitative level rated as
18 good and at a frequency higher than 85 percent. So
19 the highest-rated foodstuffs are chocolate pudding,
20 peanut butter, regular chocolate milk, yogurt,
21 et cetera, gelatin, low-fat milk, and simple syrup
22 with sour apple.

1 In terms of the components for a medkit,
2 outlining the stability of the materials of crushed
3 doxycycline in solutions in food matrices by these
4 individuals by laboratory personnel, BARDA
5 sponsored another IND study. The objective of this
6 study was to evaluate the stability of doxycycline,
7 solid, oral dosage, when dissolved or suspended in
8 tap water and then mixed with food matrices or with
9 milk and soy infant formula.

10 The testing frequency of the tap water and
11 drug mixtures was evaluated at 0, 1, 2, 12, 18, 24,
12 36, 48, and 60 hours. Doxycycline was also mixed
13 with the following foods described
14 before: chocolate pudding, the peanut butter,
15 chocolate milk, simple syrup, apple juice. And the
16 food mixtures were evaluated at 0, 1, 2, and
17 4 hours for stability.

18 The stability evaluation included assessment
19 of each drug, a compound of the drug in tap water,
20 a mixture across a pH range of 3.0 to 8.5 over a
21 temperature range of 41 to 70 degrees Fahrenheit.
22 And the analytical testing scheme resulted in 240

1 analytical samples for each drug evaluated, for
2 concentration, for degradation and impurities,
3 appearance, for the tap water, and drug mixtures.

4 The analytic scheme for the food matrices
5 resulted in some 147 analytical samples of
6 doxycycline, 144 with food and drug mixtures, and
7 three food preparations with the drug was to be
8 used as a control for degradation and impurity
9 assessment.

10 The results of the study indicate that doxy
11 remains stable in water at room temperature for up
12 to 60 hours at pH ranges from room temperature and
13 at 5 degrees from a pH of 2.75 up to 4.6. And it
14 appeared slightly less stable at neutral or highly
15 alkaline conditions, pH up to 8.5

16 In foodstuffs, the antibiotic remained
17 stable for four hours at room temperature in apple
18 juice, the simple syrup, cow's milk and soy milk.
19 And it was stable in chocolate milk for the same
20 period of time when kept at 5 degrees centigrade.
21 I might add, forget peanut butter; apparently loss
22 of recovery. It's about 86 percent at one hour, so

1 don't consider this in your future. The acceptance
2 criteria was based on these studies at 90 percent
3 or greater recovery of the target concentration of
4 the drug in the mixing matrix.

5 So the final matrices chosen for inclusion
6 in the mixing instructions that I'll describe are
7 apple juice, chocolate milk, and simple syrup.

8 We're currently in the process of
9 investigating the ability of subjects to follow the
10 written instructions for home preparation of
11 doxycycline crushing and mixing in these
12 foodstuffs, in the apple juice, chocolate milk, and
13 infant formula, as well as simple syrup. These are
14 the foodstuffs that we believe to be readily
15 available in households. And it's similar to the
16 human factor study design described by Dr. Cohen.

17 The study will be a single-center,
18 observational, performance-based study to observe
19 participants using the home preparation
20 instructions for adequate preparation; to test
21 foodstuffs mixed by the study participants for
22 homogeneity and for correct dose of the drug; 3, to

1 recommend further revisions for preparation
2 instructions if the results from either study
3 number 1 or 2 indicate that changes are needed to
4 improve user comprehension and/or that the dose
5 prepared is the dose that is available within the
6 food matrices for administration.

7 I understand, to date, 21 participants have
8 been enrolled in the study. But it's designed for
9 600 individuals total, with 100 individuals
10 representing the first responder community,
11 including, as necessary, varying literacy levels in
12 these populations. The sample regions will include
13 Baltimore City, Baltimore County, and then rural
14 areas in Maryland, from the northwest, eastern
15 shore, and rural southwest parts of Maryland.

16 Each study participant will be given -- in
17 his or her station, will be performing
18 individually, will not be able to see other
19 participants. And all participants will be given
20 the same instructions. And we can give you further
21 details of the protocol if you wish at a later
22 point in time. But their actions will be recorded.

1 Final preparations will analyze for food
2 concentration and homogeneity of the mixture.

3 We are going to now do the show-and-tell,
4 passing out to you all the current U.S. Postal
5 Service home kit examples. We will need to
6 re-collect these when we are finished.

7 [Laughter.]

8 DR. KORCH: I think they just have placebos
9 in there, if there's anything at all in the actual
10 container.

11 But this is the U.S. Postal Service example,
12 and it's a model for what we might consider for a
13 commercially produced medkit for first responders.
14 However, in describing a new kit, we would have
15 other features, for example, consideration of
16 packaging and blister packs.

17 I've also pointed out that this packaging
18 for the U.S. Postal Service was modeled after the
19 CDC packaging. But blister packs were not included
20 in this particular model for considerations for
21 cost and for ease of re-issue for expired tablets,
22 as you've heard.

1 Now, I want to stress that our proposed
2 efforts still rely primarily on open points of
3 distribution -- I've said that a few times -- as
4 planned, for providing these products to the
5 general population in the event of an emergency.

6 The medkit proposal is for the first
7 responder community and would have the following
8 components. This would be provided under
9 prescription from a family or other work-related
10 medical provider. One unit would be prescribed or
11 allowed to be filled for each household member.
12 And as with the postal model, there would only be
13 one configuration of the medkit, and this would
14 have utility for all family members by providing
15 preparation instructions, as I just described, for
16 pediatric and other household members.

17 This proposal for a forward-deployed
18 home-available medkit is also designed for
19 addressing populations' and individuals' needs for
20 the first 10 days of supply. And thereafter, we
21 would expect the entire population to have obtained
22 the balance of their anthrax post-exposure

1 prophylactic antibiotics from the established PODS
2 systems or other systems.

3 A proposed method for handling expired
4 materials would need to be outlined on the label.
5 And if possible, we would explore incentives with
6 industry partners to see about enhancing compliance
7 for disposal of expired materials by potentially
8 identifying or offering a price break on future
9 purchase of resupply for return of intact expired
10 kits.

11 Thinking ahead, we would also like your
12 opinion or recommendations on potentially
13 establishing a national registry for households or
14 individuals participating in this opportunity,
15 which, as you all know, is a traditional method
16 used for data collection for medical product use.

17 We believe that this proposed model has the
18 following advantages, both as a measure to provide
19 comfort to the first responder community and in
20 comparison to a general population scheme for
21 medkits.

22 First, this community will be relied upon

1 for the earliest support during a crisis, and,
2 similar to the postal model, providing peace of
3 mind to family members of those first responders,
4 who would be equally prepared. And this will allow
5 the community to focus on the rest of us during
6 response.

7 Secondly, I want to point out that any
8 proportion of the community that does not need to
9 report to a POD during the initial acute phase and
10 response would overall reduce the community-level
11 burden on the POD itself and would therefore
12 enhance the throughput for the POD participants.

13 Finally, identifying this population
14 provides us for a large enough market, so to speak,
15 for a commercial application and for a population
16 against which we could gather further data to
17 continue assessment of the perceived disadvantages
18 or advantages for prepositioning of supply.
19 Because the proposal is to allow for personal
20 purchase of these materials, it is also not
21 suggesting that there be an unfunded mandate to
22 local jurisdictions.

1 We already covered -- I think Ruth Lynfield
2 already covered this particular slide. That's one
3 of the advantages of going last, is that a lot of
4 what I intended to talk about has already been
5 covered. Therefore, I just want to focus on the
6 fact that with the most recent data from April 2011
7 through September 2011 and with recent returns, we
8 understand that the total number of returns from
9 this population is at 99 percent for the home kits,
10 home antibiotic kits. So I won't dwell on this
11 anymore. You heard this information already from
12 Dr. Lynfield.

13 So what about the concerns? We all have
14 them. Earlier concerns expressed about the public
15 health issues, potentially associated with making
16 medkits available to the general population, have
17 included the possibility of adverse events
18 occurring as a result of self-medication with
19 doxycycline, or are related to potential for
20 further increased antimicrobial resistance in the
21 community. We are going to be providing the
22 following information regarding those concerns.

1 So with regard to self-medication, we
2 undertook, in association and collaboration with
3 the National Library of Medicine, an evaluation of
4 references over the last 20 or so years to look at
5 adverse effects as a result of self-medication.
6 And the literature searched for the references for
7 data from such studies, from 1975 to 2010, within
8 the US were categorized into a variety of groups
9 for general subject matter, including anthrax,
10 released 2001, antibiotic regimen compliance,
11 Latino immigrant, antimicrobial use, and
12 acquisition behaviors, self-medication, emergency
13 response studies, and a variety of miscellaneous
14 categories to include antibiotics insurance issues,
15 physician antibiotic prescribing, and dental
16 prophylaxis as well, as well as patient
17 expectations for antibiotic prescribing.

18 The study data were gathered from a very
19 specific population, such as emergency department
20 patients, sexually-transmitted-disease patients,
21 college students visiting student health clinics,
22 Latino immigrants, injection drug users, and

1 individuals reporting for upper respiratory tract
2 infection.

3 In all studies, the proportion of the study
4 populations reported as having taken antibiotics
5 not prescribed by a physician to treat perceived
6 conditions, and the percentages of those ranged
7 from about 17 percent in the emergency department
8 patients to about 25 percent in injection drug
9 users and upper respiratory tract infection
10 patients.

11 Now, we're not saying that this is
12 comprehensive, that this provides us with
13 definitive information. But in general, there's
14 been fairly limited data collected over the period
15 of these years with regard to self-medication and
16 reports of events from individuals having the
17 opportunity to misuse antibiotics that are
18 currently available.

19 Regarding public health mitigation
20 strategies, there are a variety of things that
21 could be proposed to mitigate. The FDA has
22 regulations and procedures in place to monitor,

1 manage, and mitigate the risk of adverse events
2 from this and other types of misuse. As you know,
3 for most drugs, a product label and post-market
4 surveillance is all that's required to ensure that
5 the benefits of therapy outweigh the risks.

6 For certain drug classes -- we're not
7 necessarily proposing this here, but there's the
8 opportunity for risk evaluation and mitigation
9 strategies. Elements of REMS may include a
10 medication guide provided to patients along with
11 prescription and communication plans for healthcare
12 providers to support implementation of the REMS.
13 In fact, FDA is using REMS to balance the benefit
14 of prescribing controlled substances, extended-
15 release or long-duration-acting opioids, et cetera.

16 Although we do not think that doxycycline
17 falls into this category, we wanted the committee
18 to at least understand that we are aware that FDA
19 already has this tool in place if one were needed
20 to be enacted.

21 Through the Safe Use Initiative, FDA has the
22 ability to collaborate with the stakeholders to

1 reduce preventable harm by identifying medication
2 risks and developing, implementing, and evaluating
3 intervention with partners and stakeholders such as
4 CDC, pharmacists, healthcare professionals, first
5 responders, and household members.

6 Regarding misuse leading to adverse
7 effect -- and, again, part of the other study that
8 I mentioned, the literature search, touched on this
9 as well. Based on the study sponsored and
10 conducted by the CDC and the current experience in
11 Minnesota for the postal service EUA, we believe
12 that it is not very likely that doxycycline would
13 be improperly used when dispensed as a packaged
14 medkit and that it remains under the control of the
15 first responders and their families. But then
16 again, future studies need to identify this a bit
17 further.

18 The number of pills provided in the medkit
19 also reduces the likelihood of adverse effects due
20 to product misuse. It doesn't eliminate it, but we
21 think there's -- again, measureable. And the
22 ability to examine and mitigate the risk of misuse

1 leading to AEs and coupled with the expected
2 benefit and preparedness we would argue support a
3 strategy for prepositioning products with this
4 indicated population.

5 Another risk that must be acknowledged is
6 the development of resistance to doxycycline in the
7 general microbial community. Antibiotic resistance
8 has been called, of course, as you all know, one of
9 the world's most pressing public health problems.
10 And this is an issue for all antibiotics, not just
11 for doxycycline.

12 Antibiotic product labeling already cautions
13 healthcare professionals to prescribe these drugs
14 only to treat infections that are believed to be
15 caused by bacteria. Labeling also encourages the
16 healthcare professionals to counsel patients about
17 proper use. This language is currently on the
18 doxycycline package insert you see, and if
19 necessary, FDA has the ability to require post-
20 approval monitoring of the antibiotics for the
21 development of resistance. This was recently
22 conditioned for approval for antibiotics.

1 In addition, FDA has partnered with CDC on
2 Get Smart: Know When Antibiotics Work, a campaign
3 that's offered through web pages, brochures, fact
4 sheets, and other information sources aimed at
5 helping the public learn about preventing
6 antibiotic resistance infections through misuse.

7 So based on these strategies to monitor and
8 mitigate the risks of antibiotic resistance, the
9 benefit of prepositioned medkits for use during an
10 anthrax event, we also think the overall benefit
11 outweighs some of the risks of antibiotic
12 resistance in this population again.

13 In December 2010, the Assistant Secretary
14 for Preparedness Response commissioned the
15 Institute of Medicine to examine the potential
16 uses, benefits, and disadvantages of a variety of
17 strategies for prepositioning of antibiotics. ASPR
18 was seeking to identify positive and negative
19 aspects of available and hypothesized strategies,
20 including the use of commercially available,
21 FDA-approved medkits. The IOM released its results
22 in September 2011 containing findings and

1 recommendations, as identified here.

2 Although the IOM did not recommend the
3 broad use of pre-dispensed medical countermeasures
4 for the general population, they did determine that
5 targeted, predispensed, medical countermeasures
6 might be used for certain populations, such as
7 first responders who lack access to antibiotics via
8 other timely dispensing mechanisms.

9 Taking their findings into consideration, we
10 believe that the proposed strategy does address
11 their finding specifically and that targeting of
12 this particular population enhances the community's
13 ability to continue critical services by
14 potentially speeding access to prophylaxis to these
15 first-responder populations, reducing the burdens
16 on the PODS and minimizing the potential for misuse
17 in a population that is already cognizant of its
18 role and responsibility at the community.

19 Furthermore, impact on public funds, which was a
20 concern of the IOM study, is not directly affected
21 since the cost would not specifically be borne by
22 the already financially-challenged state and local

1 government.

2 So next steps or what we would hope, based
3 on your opinions and your recommendations for
4 making changes to our proposed course of action, we
5 would likely pursue the following next steps.

6 BARDA would initiate more structured
7 conversations with the drug manufacturers for the
8 commercial development of a medkit. We will
9 continue to seek guidance with FDA and you all,
10 understanding that further studies will very likely
11 be needed or repeated to satisfy regulatory
12 requirements. And then we would hold discussions
13 on the programmatic steps forward, held with our
14 own federal interagency partners and with the
15 stakeholder communities and professional
16 organizations to further refine the concepts on how
17 the kits ultimately would be prescribed and
18 tracked.

19 So in summary, to summarize my presentation
20 and our request, the proposed approach to add
21 medkits to our armamentarium of potential responses
22 to an anthrax attack, direct response to the

1 government's directives to increase our national
2 and local preparedness against such threats, this
3 medkit option that we've proposed adds to our
4 current but limited forward-deployed home medical
5 kit capabilities already piloted within the U.S.
6 Postal Service and has been evaluated with regard
7 to potential risks and benefits that have already
8 been described.

9 Again, the approach that we are describing
10 is incremental, it's measured, and it addresses the
11 needs of our community, as well as the risk and
12 benefit concerns that we are all interested in
13 knowing more about.

14 So thank you once again for the opportunity
15 to present to you our efforts and thinking
16 regarding the opportunity to increase the
17 preparedness of the nation against, as I said, a
18 low-frequency but highly significant threat to our
19 health security. At the end of the day, we are
20 looking toward every advantage that we can envision
21 to provide the entire population a way of
22 preventing large loss of life that an event of this

1 sort would produce. We need to provide for
2 preparedness in depth, and we feel that this added
3 approach will give us a greater chance to
4 responsibly protect our communities. Thank you.

5 **Questions and Clarifications**

6 DR. MOORE: Thank you, Dr. Korch.

7 We're going to move to questions and
8 clarifications of the last three presenters.

9 Dr. Erstad?

10 DR. ERSTAD: I had a question for Dr. Korch.
11 While there may be reasons for giving the medkits
12 to first responders for a variety of reasons, I was
13 curious if there was any evidence that it really
14 did increase responder willingness to report when
15 countermeasures were made available.

16 Was there any evidence from past studies,
17 for instance, that responders really do come out
18 more, if that's the case?

19 DR. KORCH: To the best of my knowledge,
20 such studies are not available, have not been done.
21 So it would be an important consideration and an
22 important piece of information. Our assumption is

1 that advantages of this sort would be. Discussions
2 with some of the communities of interest, some of
3 the first-responder professional organizations
4 suggest that this would be an appreciated approach.
5 But no. In terms of specific studies, we have
6 nothing at this point.

7 DR. MOORE: Dr. Wolfe?

8 DR. WOLFE: A couple of questions. One, did
9 your group that commissioned the IOM study disagree
10 with the IOM recommendations with respect to
11 general predispensing by going to a physician,
12 getting a prescription, and so forth?

13 DR. KORCH: We didn't disagree. I mean, the
14 information provided back to us I think was
15 balanced. Again, to characterize the IOM
16 study -- and we will have a presentation, I
17 believe, a little later on from the study. We
18 believe that their disinclination or indication
19 that there are more preferred methods took into
20 account some of these issues of increased
21 possibility of adverse effect, of misuse.

22 Also, at the time, we believe the panel also

1 thought that there would be an increase cost, that
2 the cost for this provision to the general
3 population would somehow also be passed onto the
4 local jurisdictions, which of course is a major
5 consideration, and it's not something that was
6 intended or in the description or the request to
7 the IOM that we were specifically asking about.

8 DR. WOLFE: The other question was, on one
9 hand, for very good reasons, you've identified
10 first responders -- police, fire, healthcare
11 professionals, and so forth -- as being the group
12 that might be appropriate to get this out to. And
13 on the other hand, you've said that it would not be
14 a financial burden. So the implication is that
15 these people would pay for this themselves or the
16 departments that they are working for would pay for
17 it.

18 What's the pay part of it?

19 DR. KORCH: At this point, the model that we
20 proposed would be for the individuals themselves to
21 incur the cost. That doesn't predispose or exclude
22 the possibility, were such a kit to be made

1 available, that jurisdictions themselves would
2 choose to take advantage. But there are already
3 those capabilities with regard to forward-deployed
4 caches. So at this point in time, there is nothing
5 for a jurisdiction to identify for their own
6 particular needs, the ability to engage.

7 However, it's the intent right now to at
8 least examine or explore how individuals themselves
9 would be purchasing these on a voluntary basis and
10 through physician prescription to enhance their own
11 personal preparedness in this community.

12 DR. WOLFE: It just would seem that this
13 might be a disincentive to this group that we are
14 saying is important and want them to go first, but
15 you have to pay your own way. I just think that's
16 a serious problem which needs to be resolved early
17 on because you can have a different response by the
18 first responders if they have to pay their own way.
19 It's like almost buying your own helmet or
20 something, if you're a fireman.

21 DR. KORCH: No. Absolutely. There is
22 a -- and again, depending on the price point, on

1 whatever the specific costs would be -- and this
2 would take shape as we have further discussion with
3 the industry itself on what the actual cost would
4 be for the kit. The limited information that we do
5 have, at least from the CDC study that I believe
6 you heard, was a certain price point of about \$20
7 or so. We understand from discussions with
8 Seattle, King County that the \$10 to \$20 range was
9 an appropriate set point as well for this.

10 So understanding that this, in association
11 with other things that people do in terms of
12 purchases that they make for their own personal
13 preparations, preparedness, would have to be taken
14 into account.

15 DR. MOORE: Thank you. Dr. Morrato?

16 DR. MORRATO: Thank you. I also have a
17 couple questions for you, Dr. Korch. Again, kind
18 of building on the practicality of how does this
19 get rolled out, I just want to make sure I
20 understand.

21 Is the intent, then, to go after a specific
22 narrow indication of just use in first responders,

1 and then if you were to expand beyond that, that
2 would be a new regulatory submission, et cetera?
3 Or is it just a staged launch? I've heard both
4 languages.

5 DR. KORCH: No, it's the former. At this
6 point in time, we would be looking at the
7 indication for this particular population, and then
8 further considerations after the fact would follow
9 on.

10 DR. MORRATO: With additional testing and
11 whatever might be required?

12 DR. KORCH: Exactly.

13 DR. MORRATO: Okay. That's very helpful.
14 And then in terms -- the delivery, then, would be
15 through these responder stakeholder groups who
16 might be local municipalities, it might be national
17 organizations, et cetera. Would they take on the
18 same types of responsibility that the postal system
19 is using in terms of that every-six-month follow-
20 up, or how do you envision that point?

21 DR. KORCH: The follow-up itself, at this
22 point in time, not built into our model is the

1 necessity for a specific follow-up through a
2 specific group, something that I think we could use
3 your recommendations on with regard to how might
4 that be affected.

5 As I mentioned, there are registries and
6 other mechanisms available. But because of the
7 wide distribution of these, we're talking about
8 something happening at a national level. It would
9 probably, could be handled through the physician-
10 patient relationship itself. But again, the need
11 to explore for that how one might best affect the
12 ability to follow on, to understand how to do the
13 various functions that right now currently serve in
14 the postal model. The postal model is a fairly
15 well-intact model, so it has advantages to that
16 end.

17 DR. MORRATO: Then just my last question
18 related to the postal model, then, has there been
19 consideration with what Dr. Lynfield had
20 recommended in terms of having, instead of storage
21 at home, more at the work site?

22 DR. KORCH: Certainly, it is a possibility,

1 as I mentioned before, workplace. This then would
2 be a different model. And under those
3 circumstances, procurement of those kits and the
4 deployment of those kits would completely fall
5 under the jurisdiction itself. So there are
6 possibilities for that.

7 But no. This model would -- even with
8 consideration of Dr. Lynfield's recommendations, we
9 described this as yet another layer for
10 preparedness. So that, as I indicated in my slide,
11 is a methodology that is potentially possible and
12 is actually occurring in certain localities.

13 DR. MOORE: Dr. Neely?

14 DR. NEELY: I noticed in the medkit that it
15 said that there was going to be information
16 disseminated via radio and television. Has there
17 been discussion about more modern communication
18 methods, such as social media, e-mail, internet? I
19 think that's a really critical way to disseminate
20 information and needs to be looked at.

21 DR. KORCH: We'll certainly apply not just
22 specifically to this, but at ASPR as a whole. In

1 fact, we do have a major challenge that we've
2 issued, and other activities ongoing for public
3 health emergency preparedness at large, to use
4 Twitter, Facebook, a whole variety of social media.

5 CDC also participates in this same sort of
6 outreach. And in addition to that, we know from
7 our experience, 2009 H1N1, there are other
8 communities of interest, the faith-based
9 communities. And so there are a variety of
10 communication modalities and methods, but we have
11 not ignored the real power of the current social
12 media for being able to accomplish that.

13 DR. MOORE: Dr. Vaida?

14 DR. VAIDA: Yes. With all the work being
15 done on the mixing, and stability, and trying to
16 crush the tablets, why did you go that route when
17 there is a suspension and a powder? Was it the
18 expiration dating? Was it patent? Was it cost?

19 DR. KORCH: For the most part, my
20 understanding -- this predates me. But the need
21 for simplicity with regard to providing to the
22 families, the mix and matching that suddenly

1 happens over time of developing formulations for
2 different aspects of the family unit itself becomes
3 complicated. And so in a sense -- I'll call it the
4 "Keep It Simple, Stupid" philosophy -- and I say
5 that with a great deal of respect to the
6 complexities here -- argue for the fact that if it
7 is possible to demonstrate that simple crushing,
8 mixing with household foodstuffs provides a similar
9 advantage to what would otherwise be in an oral
10 liquid formulation, we thought that that outweighed
11 the necessity to have multiple different
12 formulations provided for the household.

13 DR. MOORE: I have a related question. I
14 don't know if you can answer this or not. Why
15 doxycycline and not cipro? I mean, the point was
16 made that there are so many different formulations
17 for doxycycline, and yet we're sticking with the
18 pills, whereas my impression is that's not the case
19 for cipro.

20 Why was the choice made for doxy and not
21 cipro?

22 DR. KORCH: Again, I believe that the

1 decision to move with doxycycline was largely cost
2 related. I can refer to my other colleagues since
3 this also predates my specific -- Dr. Yeskey, would
4 you care to respond also?

5 DR. YESKEY: Yes. Thank you. This was a
6 decision that was made in response when we were
7 deciding what was going to go into the USPS medkit.
8 And it was cost related. There was also other
9 issues around ciprofloxacin as far as having a
10 broad spectrum antibiotic in a medkit for
11 resistance purposes, other safety concerns that are
12 related to the black box warning in cipro, and
13 things of the like.

14 So it was decided with HHS and CDC at the
15 time that it was probably prudent just to go with
16 doxycycline.

17 DR. MOORE: I'm sorry. I didn't identify
18 myself for the transcription. This is Dr. Moore.

19 Well, to that end, the question really is,
20 you're going to be giving doxycycline to small
21 children with the risk that that is associated
22 with. I don't know. I'm just curious as to the

1 discussion that went on with this -- I mean, I know
2 it's fine in kids, but still, I think my general
3 impression as a non-pediatrician would be the risk
4 of doxycycline to kids is low. But I daresay that
5 the risk of tendon rupture with cipro is probably
6 lower.

7 DR. YESKEY: Right. Again, the risk-benefit
8 ratio -- if there is an actual anthrax attack, the
9 risk of taking doxycycline is very low.

10 DR. MOORE: Right.

11 We have a list of others who want to
12 participate. Dr. Kaplan? Yes. Go ahead, Doctor.

13 DR. KAPLAN: As I understand it, this is by
14 prescription for the first responders. So my
15 question is, does someone go to their doctor and
16 say I'm a first responder, so I need a
17 prescription?

18 DR. KORCH: It would be envisioned that, in
19 some way, there would have to be a recognition.
20 And I'm not sure about verification. But yes.
21 Essentially, someone would need to say, "I
22 represent this community. This particular drug is

1 available for this community," and with the
2 indications and the intent for this particular
3 product. And of course this would also require
4 education of the general population of healthcare
5 workers and physicians to identify that this is the
6 intended use and the method for acquiring -- and
7 the rationale for requiring this particular
8 product.

9 DR. MOORE: Dr. Fischhoff?

10 DR. FISCHHOFF: Thank you. Thank you for
11 the interesting presentation and the work. You
12 framed the presentation in slides, I guess 8 and 9,
13 as an analysis of alternative systems for making
14 this work. And there was a lot of ambitious data
15 collection, some very interesting behavioral
16 studies.

17 I didn't have a clear picture of what the
18 overall analytical approach was, of how are you
19 going to integrate these pieces? What were the
20 performance parameters that you all are looking at
21 in terms of this? How will those parameters be
22 updated, say, with the results from the CDC in the

1 Minnesota study? How would those summaries capture
2 the uncertainties surrounding the internal and
3 external validity that the presenters gave us? And
4 then can you envision a profile of those
5 performance parameters that would lead to a
6 recommendation to whoever has to make this
7 decision, that this was not -- how would you
8 compare these things and how would you say that
9 this is actually -- we don't have an acceptable way
10 of doing this?

11 DR. KORCH: Wonderful sets of questions.
12 And to that end, as we have progressed with regard
13 to our thinking on moving this whole concept
14 forward, step number one was being able to at least
15 identify some of the criticalities of these from
16 recommendations and from issues that are identified
17 by groups like this, to then build further on into
18 the study plan, just those kinds of identified
19 needs, the integration of this particular
20 information.

21 If the opinions or if at some point in the
22 near future it is determined that this is not

1 necessarily viewed as a viable approach, the need
2 for those continued studies or the need to invest,
3 then, at the BARDA level and elsewhere within the
4 HHS community for those studies would obviously not
5 need to happen.

6 So this is our very first step out from
7 where we were to a point up to about 2009. But
8 recognizing that those types of analyses and that
9 type of data-planning integration is critical to
10 the long-term ultimate goal of, then, providing
11 this particular type of capability.

12 So wonderful questions, but at this point in
13 time, don't have a specific programmatic
14 description of integration of all of those
15 particular issues at this point, aside from what
16 you saw based on FDA guidance or FDA
17 recommendations in the 2006 to 2007 time frame
18 regarding what FDA thought might be important to
19 have by way of preliminary information for further
20 discussion of the concept.

21 Does that answer the question? I know it
22 doesn't answer your question in the detail, in the

1 level that you had hoped for.

2 DR. FISCHHOFF: So I guess maybe where I
3 would want to start would be what are the
4 performance parameters that we're looking for from
5 any of these systems, and then work backwards from
6 a model that would then integrate and be able to
7 take advantage of the different kinds of evidence
8 that you're pulling together.

9 DR. KORCH: Well, certainly we want to see a
10 continuation of information regarding the ability
11 of these populations to use these products
12 correctly, comprehension of the importance of
13 having this particular capability made available to
14 the first responder community. We'd be interested
15 in other analytics with regard to the ability of
16 this population -- or the general concept of
17 integrating user needs, as was described earlier by
18 Dr. Cohen.

19 So I'm unprepared right now to give you a
20 fully fleshed-out answer to that. But again,
21 hopefully, also with the opinion and
22 recommendations of this combined advisory group, we

1 would be able to further or more completely
2 provide, develop that particular concept or those
3 particular capabilities.

4 DR. MOORE: Thank you.

5 Dr. Huntley-Fenner?

6 DR. HUNTLEY-FENNER: Are we able to ask
7 questions of other presenters as well?

8 DR. MOORE: Well, here's the thing -- and I
9 apologize to everybody who got on the list to ask a
10 question. I want to try to restrict our questions
11 and clarifications to the speakers who just went
12 because we'll have time this afternoon to ask other
13 questions.

14 DR. HUNTLEY-FENNER: Yes. So my question
15 had to do with the Homeland Security presentation
16 and then the chart at the very end, which falls in,
17 I think, that category.

18 DR. MOORE: That's fine. Would you mind if
19 we come back to you then in the afternoon.

20 DR. HUNTLEY-FENNER: Sure.

21 DR. MOORE: Dr. Gellad?

22 DR. GELLAD: Yes. I had two quick

1 questions. The first was about, is this product
2 going to need to be repurchased every year? Is
3 that still the model that's being developed? And I
4 guess the reasoning for that, knowing the stability
5 of doxycycline over time.

6 The second question, I speak more, I guess,
7 as a concerned parent. I'll be honest.

8 I'm sorry?

9 DR. MOORE: Sorry.

10 DR. GELLAD: Maybe this is for the previous
11 speaker, but are there threats to the water supply
12 with anthrax attacks, whether inhalational or not,
13 just when you talk about the preparation of
14 doxycycline, whether workers aren't showing up or
15 direct?

16 DR. KORCH: Well, I'll attempt to answer the
17 second question first. We believe the primary
18 concern from an attack from inhalational anthrax is
19 in that first exposure to the cloud itself. With
20 regard to contamination of water supplies or water
21 sources, again, this relates primarily to the route
22 of transmission. It would be oral. It would be

1 different than the initial attack in a pulmonary
2 setting. The concentration or dilution effect in
3 the water supply would probably be overwhelming.
4 The fact that our water is treated using
5 antimicrobial materials would probably also further
6 reduce the likelihood that environmental
7 contamination of the water supply itself poses a
8 potential problem with regard to the mixing itself.

9 So your question really was, if it's in the
10 water supply, how do I know I'm not mixing anthrax
11 in, I suppose, with regard to your question.

12 DR. GELLAD: Yes. But also, it wouldn't
13 just be anthrax, but if the water supply is clean
14 for other contaminants also.

15 DR. KORCH: Yes. In general, our water
16 distribution systems and the use of chlorines and
17 other substances to reduce the microbial
18 concentration below an acceptable level probably
19 argues to the fact that the water supplies would be
20 safe.

21 The first question, again, that you asked
22 related to --

1 DR. GELLAD: Repurchasing every year.

2 DR. KORCH: Right. Again, this would be
3 based more than likely on expiry. My understanding
4 is that the materials themselves would have an
5 expiry of a considerable longer period than a year.

6 So it's again in discussion with the
7 manufacturers themselves and with the FDA as to
8 what an appropriate expiry would be. We would hope
9 it would be greater than a year for the expiry.
10 But again, that remains to be discussed. It would
11 be hoped that it would be longer than a year.

12 DR. MOORE: My apologies to
13 Dr. Huntley-Fenner. Please ask your question. I'm
14 sorry. I misunderstood. Please ask your question.
15 Thank you.

16 DR. HUNTLEY-FENNER: No problem.

17 So my questions really had to do with this
18 slide on the delayed ability to provide appropriate
19 medical countermeasures could cost lives. And
20 there's a sequence of detection and distribution,
21 dispensing.

22 Each one of those, deciding whether to

1 trigger a response, we're looking at on the order
2 of a day or two. And the steps are really
3 dependent -- in some cases dependent on one
4 another.

5 So what that brings to mind is a scenario
6 where you've got prepositioned kits in place. You
7 have a very limited time window in which to deploy
8 them and a lot of uncertainty around a series of
9 potentially local events. And you increase the
10 likelihood that there will be situations where
11 persons are taking steps without actually there
12 being a direct exposure risk, which potentially
13 affects the risk perception profile of the entire
14 population.

15 So one question we might ask, as we're sort
16 of thinking about a study is how do we assess the
17 risk perception, and how does that change the
18 targeted population, and how does that change over
19 time, given the regime that we're proposing to put
20 in place?

21 DR. KORCH: I'll let Susan Collier-Monarez at
22 least describe -- you're right. At every slice of

1 time, and the decision framework for identifying
2 when does the SNS get notified -- I mean, once that
3 trigger occurs in a local population or when an
4 event has happened, there are Bioshield-level
5 events, bars that are activated based on a certain
6 identification and verification of anthrax in
7 aerosol samples, to the extent that the Bioshield
8 machinery is available and working in the locations
9 where the event happened.

10 So we can model and we have modeled what the
11 net effect on the population would be, relative to
12 initial identification, as you saw, based on that
13 model, the descriptor there, of what time you have
14 and what capability you have to protect the
15 population, based on an initial event that's
16 identified from a Bioshield, and then what would
17 happen with the early identification of a few index
18 cases coming on in and activation of the public
19 health laboratory structure, the LRN, et cetera.

20 Each of those, of course, as you've
21 correctly identified, has a decision cycle
22 associated with it. And so as we proceed down that

1 slope, it becomes more and more critical to be able
2 to, as quickly as possible, provide materials, as
3 you saw.

4 Susan, do you want to comment any further on
5 the question?

6 DR. COLLIER-MONAREZ: No. I think you've
7 covered the main issues. I mean, one of the
8 measures that needs to be put in place following an
9 event, of course, is robust risk communications.
10 So having an understanding of the event and having
11 event characterization capabilities, including
12 BioWatch, as well as sampling in the environment,
13 and then the ability to translate that into
14 actionable public health communications to a
15 potentially effected populations -- and that's
16 certainly where the nexus between Homeland
17 Security, and the public health community, and the
18 HHS really sits, is that there are things that we
19 will be putting in place to make sure that we have
20 the most robust event characterization possible.
21 And then translating that information to CDC,
22 members of the public health community, for them to

1 be able to inform the potentially affected
2 population, to make the determination of whether or
3 not using prophylactic medical countermeasures is
4 in their best interest and the pros and cons
5 associated with that.

6 DR. KORCH: At the heart of your question,
7 though, was a very interesting question, to what
8 does the affected community understand?

9 DR. HUNTLEY-FENNER: Right. It gets to this
10 question of how do I decide whether I need to take
11 this thing or not, which is a critical piece.

12 DR. KORCH: Right. And so in this
13 particular context, we would expect the indication
14 on the label to be, "Take when told to by public
15 health or by local authorities." But the nature of
16 your question is, do people understand the
17 immediacy of that need, relative to what we just
18 described to you all, with regard to the time
19 consequences of delay to decision?

20 To the extent that in the tabletop exercises
21 that we've performed in the past -- and we've done
22 this for a number of different settings. Most

1 recently a major tabletop called Dark Zephyr was
2 run with the city Bay Area locality and State of
3 California for release of anthrax in the Bay Area,
4 including members of these various affected
5 communities, such as National Firefighters
6 Association, police, et cetera, individuals at
7 various levels.

8 For the most part, individuals in the
9 general public or even individuals in some of these
10 first responder communities have not been really
11 made aware and don't really necessarily appreciate
12 the criticality of time in this particular setting.
13 And I think that's something that really, in terms
14 of risk communication -- irrespective of this
15 particular proposal, is something we really must be
16 addressing.

17 DR. MOORE: We actually have a long list of
18 individuals who have held their hand up and want to
19 ask a question. I'm going to ask them, if
20 possible, if we can, to hold it until this
21 afternoon. And we will have access to the
22 speakers. Let me confirm, we'll have access to

1 this morning's speakers this afternoon when we ask
2 questions. Okay. That's fine. Thanks.

3 We will now take a short 15-minute break.
4 Committee members, please remember that there
5 should be no discussion of the meeting topic during
6 the break, amongst yourselves or with any member of
7 the audience. We will resume sharply at 11:00.
8 Thank you.

9 (Whereupon, a recess was taken.)

10 DR. MOORE: Let's resume our presentations.
11 So I'll have everybody take their seats. Again, my
12 apologies. We have a tight schedule, so we have a
13 lot of presenters who need to move forward today
14 just in this one session.

15 So if everyone will take their seats, we
16 will move forward. We're going to hear from Dr.
17 Robert Bass, who is ready to go.

18 Dr. Bass.

19 **Association Presentation - Robert Bass**

20 DR. BASS: Excellent. Thank you. I'm going
21 to go ahead and get started. And I want to thank
22 the panel for the opportunity to present the report

1 from the Institute of Medicine on prepositioning
2 antibiotics for anthrax.

3 DR. MOORE: Hold on a second, Dr. Bass.

4 Ladies and gentlemen, could you please
5 finish your conversations out in the hallway or
6 bring them to an end now and take your seats? I
7 would appreciate it. Thank you very much.

8 Dr. Bass.

9 DR. BASS: Thank you. This report was
10 released, as you previously heard, this past
11 September and is available for free as a PDF
12 version at the IOM website if you'd like to review
13 it in more detail.

14 The committee was a very multi-disciplinary
15 group with members from a variety of disciplines,
16 including infectious disease, public health,
17 emergency management, social work, the
18 pharmaceutical industry, and the private sector.
19 The committee process included an extensive
20 literature review, a commission paper on the cost
21 and time savings of prepositioning, and the
22 development of a mathematical model that explores

1 the relationship between the potential health
2 benefits of prepositioning and the likely costs.

3 The committee considered the continuum of
4 prepositioning strategies from a centralized
5 approach to storage, and state, regional, and local
6 caches, as well as predispensing, which is defined
7 as storage by the intended user.

8 While potentially having the greatest
9 benefit in reducing the time to first dose, used as
10 a broad public health strategy, predispensing would
11 engender the highest relative risk and the greatest
12 cost of the prepositioning strategies. However,
13 the benefits, risks, and cost of prepositioning may
14 be impacted by the objective and the design of the
15 strategy, as well as the form of the product.

16 For example, the use of prepositioning as a
17 broad public health strategy, while potentially
18 associated with the greatest benefits in reducing
19 the time to the first dose, would be associated
20 with the greatest health risks and costs.

21 Targeting only certain subpopulations would reduce
22 both the risk and cost. Making the antibiotic

1 available for individual purchase reduces the cost
2 to the public.

3 Predispensing strategies that include
4 financial incentives and greater supervision are
5 likely to be associated with less risk but greater
6 cost. And finally, the cost and possibly the
7 health risk would be impacted by the form of the
8 product, the FDA medkit being the most costly
9 approach. We will explore these issues in more
10 specific detail in a few minutes.

11 I would like to walk you through a few key
12 elements of the report, including the decision-
13 aiding framework developed by the committee, more
14 detail on the benefits, risks, and costs of
15 prepositioning strategies, and the committee's
16 recommendations specific to medkits.

17 The committee felt strongly that there was
18 no one-size-fits-all approach to prepositioning
19 strategies. The decision-aiding framework is a
20 tool that may be used by the communities to make
21 decisions on what particular prepositioning
22 strategies may be most appropriate for them. The

1 framework has three components, assessments of risk
2 and current capabilities, ethical principles, and
3 assessment of prepositioning strategies.

4 The community's assessment of risk and
5 current capabilities includes an assessment of
6 their risk of attack -- this would likely be done
7 in conjunction with state and federal
8 partners -- an assessment of their detection
9 capability, and finally, an assessment of their
10 dispensing capability.

11 A key finding of the committee, after a
12 detailed review of the limited data on human
13 inhalational anthrax as well as interviews with
14 subject matter experts, was that the incubation
15 period for inhalational anthrax can be expected to
16 be four to eight days or longer. If jurisdictions
17 are capable of detecting an attack, deciding to
18 treat, and dispensing within 96 hours, there is
19 less justification for the additional cost and
20 potential health risk of predisposing home
21 antibiotics.

22 The second part of the decision-aiding

1 framework involves the incorporation of ethical
2 principles. The committee's analysis of the
3 ethical aspects of prepositioning strategies was
4 favorable. However, a final decision on whether an
5 individual should maintain home stockpiles requires
6 a full community assessment of factors discussed in
7 the report, including the risk of attack, their
8 detection and dispensing capabilities, the health
9 risks associated with potential misuses, cost,
10 effectiveness, and finally, the reduced flexibility
11 of the overall strategy, should the strain be
12 resistant to the particular antibiotic that is
13 predisposed.

14 The final element of the decision-aiding
15 framework is the evaluation of prepositioning
16 strategies. What are the potential benefits, such
17 as reducing the time to treatment, as well as the
18 health risks, such as the potential for misuse?
19 Can this strategy be practically applied? And
20 finally, what are the costs?

21 There are two questions for the forum today,
22 to which the committee's report provides guidance.

1 Should the antibiotic be stored in the home for
2 protection against anthrax? And the second
3 question, for those specific cases where the
4 committee found that antibiotic storage in the home
5 may be appropriate, should this be done using a
6 medkit or a standard prescription? Before
7 providing the committee's recommendations on these
8 two questions, I would like to review a few
9 relevant findings and recommendations.

10 Generally, prepositioning strategies will
11 reduce the time to prophylaxis. In this modeling,
12 the committee assumed that predispending is the
13 fastest strategy when comparing it to other
14 prepositioning strategies. On the other hand,
15 those predisposed antibiotics would not be
16 effective should the strain of anthrax be resistant
17 to the antibiotic that is predisposed.

18 There are many potential safety concerns to
19 consider with predispending strategies.
20 Inappropriate use would result in adverse events,
21 antibiotic resistance, and drug interactions.
22 Improper storage and disposal; the antibiotic might

1 not be available or would be degraded when needed.
2 Inappropriate use during a non-anthrax incident,
3 such as a white-powder event or a distant anthrax
4 attack, ineffective prophylaxis for an attack with
5 a resistant strain.

6 While predispending strategies may reduce
7 the time to prophylaxis, it should be pointed out
8 that other prepositioning strategies may be equally
9 effective at lower potential risk and cost.

10 Published data on antibiotic misuse suggests
11 that misuse of predisposed antibiotics is likely
12 to be high in the general population. The study in
13 St. Louis and the postal pilot in Minneapolis-
14 St. Paul demonstrated a relatively low rate of
15 misuse, but the committee questions whether those
16 findings can be generalized due to the unique
17 aspects of those two studies that include financial
18 incentives, short-term follow-up, and employer
19 supervision.

20 There are no available data on whether
21 medkit labeling and packaging would reduce the rate
22 of inappropriate use relative to standard

1 prescription. So a significant question remains as
2 to whether the predispensing of medkits would more
3 closely reflect the relatively low rate of misuse
4 of the two studies we just mentioned or a
5 relatively higher rate of prescription antibiotic
6 misuse that we've seen in the general population.

7 In terms of cost, generally speaking, the
8 closer that the medical countermeasures are
9 positioned relative to the intended user, the
10 greater the cost, principally due to the need to
11 manage a greater number of stockpiles.

12 Calculations were included in the
13 committee's report on the cost of its predispensing
14 program for the Minneapolis-St. Paul area. The
15 cost of predispensing for the general public would
16 be significantly higher than the cost of strategies
17 relying on points of distribution, or a combination
18 of PODS plus workplace caches, or hospital caches.

19 The committee assumed that the public health
20 agencies would not experience cost savings if
21 individual citizens could purchase home medkits, as
22 public health would likely still have to plan to

1 dispense to the entire population, for example,
2 should there be a strain resistant to the
3 antibiotic that was prepositioned.

4 Another factor the committee considered are
5 the additional costs associated with an
6 FDA-approved medkit versus a standard prescription.
7 These would include development costs, packaging
8 costs, insurance coverage, and market consideration
9 of the business case for such a product when a
10 low-cost, generic equivalent is already available.

11 Next, I'd like to move onto the
12 recommendations specific to the medkits. And
13 again, going back to the two questions, the first
14 question is, should antibiotics be stored in the
15 home to protect against anthrax?

16 In public health planning efforts, states,
17 local jurisdictions, and tribal jurisdictions
18 should give priority to improving the dispensing
19 capability of points of dispensing and push
20 strategies into developing forward-deployed or
21 cache prepositioning strategies.

22 The committee does not recommend the

1 development of public health strategies that
2 involve broad use of predisposed medical
3 countermeasures for the general population. In
4 some cases, however, targeted, predisposed medical
5 countermeasures might be used to address specific
6 gaps in jurisdictions' dispensing plans for certain
7 subpopulations that lack access to antibiotics via
8 other timely dispensing mechanisms. These might
9 include, for example, some first responders,
10 healthcare providers, and other workers that
11 support critical infrastructure as well as their
12 families.

13 Personal stockpiling might also be used for
14 certain individuals who lack access to antibiotics
15 via other timely dispensing mechanisms, for
16 example, because of their medical and/or their
17 social conditions, and who decide in conjunction
18 with their physicians that this is an appropriate
19 personal strategy. This is allowed under current
20 prescribing practice and would usually be done
21 independently of a jurisdiction's public health
22 strategy for dispensing medical countermeasures.

1 To the second question, for those specific
2 cases where the committee finds that antibiotics
3 storage in the home may be appropriate, should this
4 be done using a medkit or a standard prescription?

5 The committee does not recommend the
6 development of an FDA-approved medkit designed for
7 prepositioning for an anthrax attack until and
8 unless research demonstrates that medkits are
9 significantly less likely to be used
10 inappropriately than a standard prescription and
11 can be produced at costs comparable to those of a
12 standard prescription antibiotic.

13 For additional information, you're invited
14 to go to the Institute of Medicine website under
15 anthrax readiness. And I'd like to thank Clare
16 Stroud for her leadership during the IOM committee
17 and for her assistance in preparing this
18 presentation today.

19 DR. MOORE: Thank you, Dr. Bass.

20 We'll now hear from Dr. Pavia.

21 **Association Presentation - Andrew Pavia**

22 DR. PAVIA: Good morning. My name is Andrew

1 Pavia. I'm a chief of pediatric infectious
2 diseases at the University of Utah. I'm here today
3 representing the Infectious Disease Society of
4 America. I have no conflicts to disclose, although
5 I should disclose both that I was a member of the
6 IOM committee and that I have no vested interest in
7 the outcome of today's basketball championship.

8 [Laughter.]

9 DR. PAVIA: We appreciate the opportunity to
10 comment on the potential development of an
11 FDA-licensed medkit containing doxycycline for home
12 stockpiling in the event of an anthrax attack. And
13 you'll notice that I am trying to cure myself of a
14 PowerPoint dependency that many of us share.

15 We appreciate the need to have an effective
16 system that will allow complete dispensing of an
17 effective countermeasure within 48 hours of the
18 detection of an anthrax attack. To this end, we
19 support efforts to improve forward positioning and
20 to improve the dispensing systems. We also
21 recognize the special needs of the first responder
22 community and the need to have systems that provide

1 effective dispensing to those who will respond to
2 an attack.

3 However, the most effective systems will be
4 those that are adapted to local situations and not
5 a one-size-fits-all approach. Effective systems
6 will likely use many strategies and will take into
7 account the local capacities for other dispensing
8 and the risk. This likely will include such
9 measures as workplace dispensing, that Dr. Lynfield
10 alluded to, and closed PODS, and also include
11 discussion of vaccines.

12 Sound principles must guide the choice of
13 countermeasure dispensing measures. These include
14 balancing the incremental risks of a strategy with
15 the incremental benefits, and ensuring equity of
16 access and sound stewardship of biodefense and
17 other public health resources. And among the
18 public health resources is the viability of our
19 limited supply of antibiotics in the future.

20 At issue here, then, is really whether the
21 incremental benefits of a home-stockpiling strategy
22 outweigh the incremental risks compared to other

1 effective strategies that might include workplace
2 dispensing. It also must be multiplied by the
3 concept of the number of people at risk. So if one
4 dispenses to a very large number of people to allow
5 an effective home-stockpiling strategy, how does
6 that risk compare to a targeted response at the
7 time of an event?

8 So the calculus, then, can be thought of the
9 additional benefit times the probability that will
10 ever be needed, balanced against the risks and
11 costs specific to home stockpiling. Thus, while
12 home stockpiling or home dispensing may fill
13 certain specific needs, we have grave concerns
14 about the pathway of an FDA-licensed medkit that
15 appears to be allowing for the possibility of its
16 use as a broad strategy in the future.

17 Home stockpiling of antibiotics, including
18 the use of an FDA-approved medkit, raises a number
19 of questions which we have to think very carefully
20 about. The incremental benefit of home stockpiling
21 relative to workplace caches, postal distribution,
22 and other effective dispensing mechanisms remains

1 unclear, although there are potential benefits.

2 The risks of placing a large amount of
3 antibiotic in homes are clearly significant. We
4 can't quantify all of those risks from the
5 available data, but we need to think about each
6 individually. And these include, to what degree
7 will people access and take antibiotics that they
8 have in their home appropriately when instructed
9 and refrain from taking them when inappropriate or
10 for other illnesses?

11 There are unanswered questions about whether
12 doxycycline tablets are an effective way to treat
13 children, and any home-stockpiling strategy must
14 include something that will actually work and be
15 effective for the treatment of children.

16 The risks of inappropriate use -- and we
17 can't ignore the fact that some degree of
18 inappropriate use will occur -- include adverse
19 events. And these range from allergic type
20 reactions -- you have to recall that 145,000
21 emergency department visits each year are estimated
22 to be due to adverse events from antibiotics. And

1 they range at the other end of the extreme to
2 Clostridium difficile infections, which
3 particularly which, particularly with current
4 strains, can be life-threatening.

5 The other important risk is the risk of
6 resistance. And we need to remember that
7 tetracycline, while it does not have a primarily
8 role in the treatment of many human diseases,
9 resistance to tetracycline travels, for the most
10 part, on multi-drug-resistant plasmas. And so
11 selection for tetracycline resistance may drive
12 resistance for other agents.

13 Another issue that was alluded to briefly is
14 replacement of outdated drugs and the safe disposal
15 of those drugs. If you were to imagine 10 million
16 medkits being dispensed, as proposed by BARDA, that
17 means that with a one-year expiry, 22 tons of
18 doxycycline must be safely disposed of each year
19 and not flushed into the water supply.

20 The IOM report also raised significant
21 doubts about the cost effectiveness of seeking FDA
22 licensure and passing the costs of the licensure

1 process onto the ultimate end user, whether it be
2 the individual or the organization for which they
3 work.

4 As noted in the IOM report, the research
5 that's been conducted today, which you've heard a
6 little bit about, is really inadequate to answer
7 many of these questions. This St. Louis study had
8 rather short follow-up, a maximum of eight months
9 and a median of less than six. And the Twin Cities
10 study collected limited data on what was initially
11 384 participants.

12 So we suggest the following research and
13 development priorities. Develop and evaluate a
14 variety of methods of rapid dispensing to the
15 target population of first responders, including
16 work-based dispensing compared to home dispensing.

17 Assess the costs and effectiveness of
18 different strategies so that we can make rational
19 decisions among them.

20 Develop plans for the safe disposal and
21 replacement of home-stockpiled antibiotics; and
22 conduct detailed evaluations of the feasibility,

1 safety and efficacy of home medkits, including the
2 ability to store and find the countermeasure across
3 a variety of populations and education levels; the
4 ability to follow and comprehend instructions for
5 use; the ability to accurately prepare pediatric
6 dosing; and if necessary, consider the use of an
7 alternative pediatric formulation in the medkit;
8 and the probability and risk factors for
9 appropriate use with the proposed type of
10 packaging.

11 Lastly, any efforts that are put into
12 developing a doxycycline response should not come
13 at the expense of preparation for a response to an
14 antibiotic-resistant anthrax attack, which is a
15 very real possibility, which largely remains an
16 elephant in the room, which we don't like to
17 discuss. Thank you very much.

18 DR. MOORE: Thank you, Dr. Pavia.

19 We'll next hear from Dr. Herrmann.

20 **Association Presentation - Jack Herrmann**

21 MR. HERRMANN: Good morning. On behalf of
22 the National Association of County and City Health

1 Officials, NACCHO, an organization which represents
2 the interests of the nation's 2800 local
3 governmental health departments dedicated to
4 ensuring the conditions that promote health and
5 equity, combat disease, and improve the quality and
6 length of our lives, we'd like to thank the Food
7 and Drug Administration for inviting our comments
8 on the feasibility of an FDA-approved home medkit
9 containing doxycycline as a public health strategy
10 in the event of an anthrax incident.

11 These comments have been formed by anecdotal
12 discussions with NACCHO members and does not
13 necessarily represent a formal policy or position
14 on the feasibility of an FDA home medkit.

15 Bacillus anthracis, the bacterium associated
16 with the anthrax disease, is considered to be one
17 of the most serious potential bioterrorism agents
18 to exist and a threat to our national security.

19 The federal government has given significant
20 attention over the years to identify ways to
21 prevent or mitigate an anthrax attack such as that
22 the U.S. experienced in the fall of 2011. Equally,

1 those in the public health and medical communities
2 have been challenged to find ways to provide the
3 medical and public health response necessary to
4 minimize the morbidity and mortality associated
5 with this deadly disease, should an attack occur.

6 Local health departments find themselves at
7 the center of this challenge. All disasters start
8 and end locally, requiring these governmental
9 agencies to have robust disaster plans and stand
10 ready to respond.

11 The creation of the Strategic National
12 Stockpile, the Cities Readiness Initiative, and
13 other federally supported programs have provided a
14 critical and necessary resource for localities to
15 assist them in developing plans for the
16 distribution and dispensing of mass medical
17 countermeasures in a timely and efficient manner in
18 the aftermath of a bioterrorism incident like
19 anthrax. To date, points-of-dispensing models and
20 the U.S. Postal Service plan have been the primary
21 mechanism locals look to in addressing this
22 challenge.

1 In 2005, the concept of prepositioning a
2 medkit containing pharmaceuticals in the homes of
3 the public or select individuals such as first
4 responders was identified as a possible modality
5 for making life-saving medications rapidly
6 available and accessible. Officials representing a
7 variety of professional disciplines acknowledge
8 that the access to such a medkit containing, in
9 this case, doxycycline could address the challenges
10 of how to treat or provide prophylaxis to a large
11 population in the aftermath of an anthrax attack.
12 However, public health representatives and those
13 from the medical profession have warned that such
14 an intervention needs to be carefully assessed and
15 evaluated in order to understand the associated
16 risks and benefits of such an approach.

17 Over the past four or five years, the
18 federal government has sought the feedback and
19 comment from the public health community on the
20 viability of medkits. Throughout all of these
21 efforts, central themes have emerged: the
22 potential for premature or misuse of these kits,

1 unintentional or accidental ingestion of the
2 contents of these kits, especially children,
3 confusion regarding pediatric or other vulnerable
4 population dosing, and potential adverse reactions
5 in those taking the medication, especially for
6 those in which the use of such meds are
7 contraindicated.

8 While studies addressing some of these
9 issues have been undertaken and show some promising
10 results, these results may have been influenced by
11 a variety of factors, many of them lacking
12 sufficient power to be representative of all or
13 select populations.

14 For example, studies have been done with
15 both the general public and responder groups to see
16 if households are able to preserve the use of the
17 kits and return them when requested. Those studies
18 showed positive results, with the vast majority
19 able to return the kits intact and not
20 inappropriately using them. However, in the
21 general public study, study recipients were
22 financially compensated for their participation.

1 To date, all studies associated with
2 assessing the use of home medkits have not included
3 the stress associated with a real-time event as a
4 factor in the study. Public health officials ask,
5 if individuals were faced with a situation of an
6 anthrax incident occurring in another part of the
7 world or in a part of this country that posed no
8 perceived risk to them, would they prematurely take
9 the medication prior to the advisement of a public
10 health official, and what impact would that have?

11 One may point to a relatively recent
12 incident as a corollary for an answer. In the
13 early days following the Fukushima nuclear accident
14 in Japan, thousands of individuals not directly
15 impacted by the event went in search of potassium
16 iodide tablets, creating significant demand that
17 exceeded the stock of one leading supplier. Such
18 increase in demand occurred despite reassurance
19 from U.S. public health officials that individuals
20 were in no jeopardy of being harmed by this event.

21 Other concerns expressed by local public
22 health officials, should home medkits be readily

1 available to the public or select subpopulations,
2 include the legal challenges associated with
3 prescribing these kits, the ability to conduct
4 appropriate screening and assessment of those
5 receiving the kits, the logistics concerning
6 storage, tracking, expiration date monitoring, and
7 the replacement and disposal of expired kits, the
8 cost of the kits, and perceived ethical and
9 inequity issues associated with populations not
10 able to afford the kits, and adequately educating
11 the recipients of these kits.

12 In September 2011, the Institute of Medicine
13 issued a report, Prepositioning Antibiotics for
14 Anthrax, with local public health representation on
15 the committee that reviewed the available data in
16 preparation of this report. The report cites many
17 of the concerns identified by local public health
18 professionals and others associated with the
19 potential use of home medkits as a prepositioning
20 strategy.

21 NACCHO supports the findings of the IOM
22 report and the Institute's recommendations,

1 including that recommendation that in some cases,
2 targeted predispensing of antibacterial drugs to
3 first responders, healthcare providers, or
4 individuals who may lack timely access to such
5 drugs might be used. If the committee's meeting
6 today agree to pursue such a targeted strategy,
7 NACCHO supports a proposed label comprehension,
8 self-selection, actual-use, and human factor
9 studies.

10 Local public health department officials
11 believe that it is critical that the intended
12 recipients of these medkits understand when and
13 when not to use these kits, possess the knowledge
14 and ability to prepare the appropriate medication
15 dosages as in the case of pediatric usage, and
16 possess the understanding and ability to identify
17 and report any adverse reactions associated with
18 taking these medications contained in these kits.

19 In addition, local public health departments
20 must be included in the planning for the
21 implementation of these medkits in their
22 jurisdictions, with the understanding that such

1 agencies have limited resources and will not be
2 able to take on the sole responsibility of the
3 distribution, monitoring, tracking, replacing, and
4 disposal activities associated with the provision
5 of the kits.

6 Finally, efforts must also be undertaken to
7 address and resolve the potential ethical and
8 financial consideration if the cost of these kits
9 are expected to be transferred to the recipient of
10 the kit. Thank you.

11 DR. MOORE: Thank you, Mr. Herrmann.

12 We'll now hear from Mr. Blumenstock.

13 **Association Presentation - James Blumenstock**

14 MR. BLUMENSTOCK: Good morning. On behalf
15 of the Association of State and Territorial Health
16 Officials, ASTHO, I want to thank the FDA and the
17 greater HHS family for this opportunity to share
18 the state and territorial public health perspective
19 as you carefully and openly examine the public
20 health indications of a prescription doxycycline
21 medkit intended for post-exposure prophylaxis in
22 response to an anthrax terrorism event.

1 ASTHO is a national non-profit organization
2 representing the state and territorial public
3 health agencies in the United States, the U.S.
4 territories, and the District of Columbia, as well
5 as over 100,000 public health professionals these
6 agencies employ. ASTHO's members, the chief health
7 officials of these 59 jurisdictions, strive to
8 formulate and influence sound public health policy
9 and ensure excellence in state-based public health
10 practices across the country.

11 At the outset, it is important for me to
12 state that ASTHO does not have a formal policy or
13 position on the use of medkits. As such, my
14 comments are grounded in large part by the relevant
15 discussion, past and present, of our members
16 regarding the pros and cons of such an approach for
17 medical countermeasure dispensing.

18 There is a clear recognition by state and
19 territorial public health officials of the
20 imperative need to explore all, I repeat all,
21 feasible, practical, and safe options for rapid
22 medical countermeasure distribution and

1 administration through rigorous examination of the
2 scientific and medical benefits, the risk
3 quantification, and the tradeoffs of various
4 options, public acceptance and confidence in the
5 various strategies and tactics, and the probability
6 of such a threat justifying such varied approaches.

7 State and territorial health officials have
8 and continue to share the concerns raised in the
9 June 2008 letter from the National Biodefense
10 Science Board to the then-HHS Secretary Levitt and
11 ASPR Vanderwagen on home stockpiling of antibiotics
12 for use during an anthrax attack. Furthermore, we
13 believe that the relevant recommendations contained
14 in the September 2011 IOM report on prepositioning
15 antibiotics for anthrax clearly articulate the most
16 important priorities and concerns on the part of
17 the public health community at this time.

18 As Dr. Bass had summarized for you, the two
19 or three main issues that I want to stress here
20 today regarding home kits is the fact that priority
21 must be given to improving dispensing capabilities
22 and prepositioning strategies, such as forward-

1 deployed or cached medical countermeasures. And,
2 again, this has great reliance on a strong and
3 robust public health infrastructure as well as
4 strong partnership and utilization of private
5 sector resources. Second, however, in some cases,
6 as previously mentioned, strategic predisposing to
7 targeted populations might very well be beneficial.

8 Lastly, approval of medkits must be
9 supported by additional safety and cost research.
10 We as an organization certainly represent and
11 recognize the value of bifurcating the public, if
12 you will, into the category of first responders and
13 clinicians versus general population for the
14 purposes of exploring dual-track studies and
15 examination.

16 As such, ASTHO respectfully recommends that
17 a full suite of studies be conducted in order to
18 attempt to address the paramount safety and cost
19 concerns raised by the IOM and many of my other
20 colleagues this morning. This would include the
21 conduct of label comprehension studies, self-
22 selection studies, actual-use studies, and human

1 factor studies.

2 In closing, I'd like to share also three
3 additional suggestions or recommendations. The
4 first is benefitting and learning from prior
5 experiences.

6 As Jack had mentioned, with potassium
7 iodide, KI, with the response to the Fukushima
8 disaster, there's another element here with KI.
9 States that are host communities to nuclear power
10 plants have been prepositioning KI in the community
11 for well over a decade. So clearly, there is great
12 opportunity to learn not only public behaviors,
13 beliefs, but also those that are the operational
14 and logistical challenges of governmental public
15 health agencies with regard to the provision of KI
16 in the home, in schools located within emergency
17 planning zones, as well as large employer sites.

18 Secondly, I had the privilege of appearing
19 before you, I believe about two and a half years
20 ago, when you had a similar examination on the use
21 of Tamiflu. I believe Roche Pharmaceuticals was
22 the petitioner in response to pandemic influenza.

1 Similar studies I believe were conducted or at
2 least initiated; and while those results I do not
3 believe, are public, I would hope that this
4 committee would have the benefit of that work that
5 was conducted over the last several years,
6 recognizing it's a different medical
7 countermeasure, different threat agent. But I
8 think clearly, in some of the studies, especially
9 with societal and public behavior issues, there may
10 be some great transferrable information that we can
11 glean from there.

12 Second point, again, having the opportunity
13 with respect to Dr. Korch's question regarding the
14 notion of a national registry, whether it be
15 voluntary or mandatory, ASTHO would totally,
16 wholeheartedly support that provision and this
17 process. It provides great opportunity for
18 continuing virtual real-time follow-up with those
19 individuals that possess medkits. It provides the
20 opportunity for messaging should a real event take
21 place; so again, as a supplemental or companion
22 information that would normally come out from a

1 public health agency. And lastly, in some
2 respects, it gives public health agencies
3 visibility on what segment of their population are
4 actually potentially protected by this route of
5 medical countermeasure dispensing.

6 The last point, which relates to my previous
7 point, is the issue of things that have to be done
8 for the public health community to have greater
9 visibility on exactly what portion of the
10 population medkits will be covering.

11 Dr. Korch, again in his comments, made
12 reference to it being a little sliver. Well,
13 obviously, from the state and territorial public
14 health perspective, for planning purposes, you need
15 to know, number one, does that sliver exist all in
16 your jurisdiction; and secondly, if so, what
17 percentage of the population could be safely
18 planned to be covered through this modality as
19 opposed to the other typical or traditional
20 operations.

21 Lastly, like NACCHO and my colleagues, ASTHO
22 stands ready to provide whatever support and

1 assistance that we can do as you move forward on
2 this. As is the case everywhere, the devil is in
3 the details. And moving forward with an approval
4 of a medical countermeasure is one thing, but the
5 operational and practical field parameters that
6 need to be in place to effectively execute,
7 monitor, and benefit from the success of that is
8 critically important. And the state and
9 territorial public health agencies would play a
10 critical role and I believe a critical partner in
11 this process as well.

12 So thank you very much for this opportunity.

13 DR. MOORE: Thank you, Mr. Blumenstock.

14 Let's now hear from Dr. James.

15 **Association Presentation - James James**

16 DR. JAMES: Good morning and thank you for
17 the invitation. In case you've been PowerPoint
18 deprived in the past few minutes, I've decided to
19 reacquaint you with that.

20 Like Jim said, I want to reiterate a couple
21 of things. Number one, I am with the American
22 Medical Association, but they do not have official

1 policy on this. My remarks are made in the context
2 of the work I do at the AMA, which is preparedness
3 and response.

4 The second remark that Jim made I just want
5 to underscore is all of the studies we've looked at
6 here today, or at least the ones I've heard about,
7 are not real event studies. And I really think we
8 need to look at the real events. And real events
9 have happened with anthrax in the past, and I think
10 they have some lessons to give us.

11 I do want to say I have no conflicts of
12 interest, but I do have a lot of concerns of
13 interest, where we go with both pre-event and post-
14 event treatment of anthrax.

15 So I'd like to get a little help from my
16 friends. What's past is prologue. And where
17 anthrax is concerned and policies regarding
18 anthrax, I very strongly feel we need to look to
19 the past. And we actually have an
20 aerosolized -- it wasn't an attack; it was an
21 accidental release of a large amount of weaponized
22 anthrax spores in Russia in 1979. We don't know

1 the exact population exposed, but the population
2 living in the area where the accident occurred was
3 1.2 million. Of that, they estimated about 7,000
4 were in the immediate vicinity of the factory that
5 released the plume. Of that, of the people working
6 in that particular area, there was an attack rate
7 of 2 percent.

8 Again, we don't really know the denominator,
9 but those attack rates are far less than the ones
10 that come from our 5 pounds of Domino sugar that we
11 always hear about.

12 When you look at the total 77 cases that
13 actually died with pulmonary anthrax, another
14 interesting observation was no one was under the
15 age of 25. And there's no reason to believe that
16 children were excluded from the exposure.

17 What I really want you to look at are the
18 timelines. And the timeline is on this slide here,
19 where the exposure occurred on 2 April. There was
20 no confirmation that it was anthrax until 11 April.
21 Can we do better today? We did a lot better in
22 Florida. We had it identified and confirmed within

1 a couple of days.

2 The important thing is how fast do cases and
3 deaths start to occur. And again, this is material
4 that was published in Science from an evaluation
5 on site, conducted by folks in Harvard and other
6 areas, looking specifically at the 77 individuals
7 with hospital-recorded deaths. Looking at the
8 slide, approximately one-third occurred within the
9 first week.

10 Now, there are two ways to look at that.
11 You're going to lose one-third if you don't get the
12 material out there fast enough. But at the same
13 time, you have a week before two-thirds are
14 affected. Again, statistics can say all sorts of
15 things. But what's extremely important -- Dr. Bass
16 said that the incubation period was 4 to 7 days, I
17 believe. The first cases appeared here in two
18 days. The first death occurred in four days.

19 Anthrax usually has a prodrome. If you
20 don't get the antibiotic in during the prodrome,
21 you're too late. By the time the person has
22 developed fulminant anthrax, antibiotics are not

1 going to be that helpful.

2 Going back to Shakespeare, it is certainly
3 better to be three hours too soon than a minute too
4 late when we're dealing with something like
5 anthrax. So today, we want to look at medkits and
6 prepositioning of doxycycline.

7 Home positioning, some of the concerns.
8 Equity. People who tend to have income, insurance,
9 et cetera will certainly avail themselves of this
10 type of thing, and will we truly achieve equity?

11 Expiration dates have been discussed;
12 changes in family composition over time. You may
13 have two or three children at home today and none a
14 year from now.

15 What really concerns me is the false sense
16 of security we may give people. How fast are we,
17 A, going to detect that there's been an attack?
18 And if it's in less than a day, I would truly,
19 truly be amazed. Then you have to identify what
20 you're being attacked with. And then thirdly, is
21 it resistant to what you've prepositioned? And
22 then finally -- and this is not small. I was in

1 Florida during anthrax. I was the head of the
2 public health department at Miami. Getting to
3 declare that that was an attack was no easy matter,
4 and it didn't happen in one or two days.

5 Then there's the human factor.
6 Communication. I wouldn't care in Miami if people
7 had doxycycline at home. Cipro was in the news,
8 and they wanted cipro. And I doubt very much if
9 they could have discerned the differences between
10 the efficacy of cipro and doxycycline.

11 I think one thing we have not talked enough
12 about today -- and I don't represent pharmacies,
13 but we have 61,000 local pharmacies that could be
14 used in some sort of a prepositioning effort. We
15 could, A, rotate stocks, hopefully. You can
16 provide alternate countermeasures in case
17 doxycycline isn't the one you're really interested
18 in. And finally, I think you can do a better job
19 with equity and certainly accountability.

20 In finishing up, I just want to talk about
21 risk determination. Every time you ask the
22 question, is there a real risk, the official answer

1 is, well, we're not really sure; yet, we've been
2 evaluating this approach for seven years now. The
3 amount of public fund that's been expended on it is
4 probably in the total of fairly high, and we still
5 don't know that risk factor.

6 But one thing I have truly come to believe,
7 from my experience and reading the literature as
8 extensively as I can is, if you have a high enough
9 risk of an anthrax attack, then you should be
10 considering at least voluntary vaccination. We've
11 had effective vaccination for anthrax for over 120
12 years. It's been proven in the industrial area,
13 the commercial area, the military area, but yet
14 we're reluctant for the public.

15 I think the study that needs to be done is
16 how acceptable is it truly to the public. We know
17 how acceptable it is to the very vocal anti-
18 vaccination groups, and those are the people we
19 always hear from.

20 Thank you.

21 DR. MOORE: Thank you, Dr. James. Let's
22 move onto Mr. Topoleski.

Association Presentation - Christopher Topoleski

MR. TOPOLESKI: Good morning. My name is Christopher Topoleski. I'm the director of federal regulatory affairs at the American Society of Health System Pharmacists. ASHP represents pharmacists who practice in hospitals and health systems. The society's more than 35,000 members includes pharmacists and pharmacy technicians who practice in a variety of health settings, including inpatient, outpatient, home care, and long-term care.

I appreciate the invitation to present the views of ASHP on the evaluation and distribution of a prescription doxycycline medkit. ASHP commends the efforts of the committees for their continued study of the approaches that would facilitate timely and effective distribution of antibiotics to treat exposure to anthrax.

My comments today will focus on whether or not the distribution of doxycycline is appropriate for home use and a perspective on distribution methods for further study. Of immediate concern is

1 the availability of doxycycline. A doxycycline
2 injection is currently in shortage, which means
3 that other forms and doses of the product,
4 including oral, may be used in its place. Also
5 important to note is that tetracycline capsules are
6 in shortage currently, and manufacturers cannot
7 provide a resupply time frame at this current
8 point.

9 Both tetracycline and doxycycline are used
10 for a number of diseases, including Lyme disease.
11 In its absence, levels of doxycycline may be
12 depleted faster and to a lesser or further degree
13 than is currently projected. Therefore, this
14 product may not be the most feasible basis for a
15 medkit at the current time. Additionally, if the
16 nation were to be exposed to a doxycycline-
17 resistant strain of the anthrax spore, medkits
18 would be largely ineffective or the presence in the
19 home provide a false sense of security to the
20 general population. Coupled with the potential for
21 misuse, we may not have an abundance of doxycycline
22 to support the concept of a long-range medkit for

1 all homes in this U.S.

2 Home stockpiling of medkits in general has
3 been proposed based on the positive findings of a
4 number of studies. For instance, a CDC study
5 demonstrated that participants appropriately
6 followed instructions regarding storage and
7 reserving the emergency medkit until further
8 directed. However, the results may not be
9 applicable to the nation's public at large, as it
10 may be more difficult to give explicit instructions
11 once you initiate the treatment due to the regional
12 nature of an anthrax attack and the generalized
13 symptoms that may hinder quick diagnosis.

14 Due to public fear, misinformation, and
15 miscommunication, patients may use the medkit
16 supplies for prophylaxis under circumstances when
17 they may not have been properly evaluated for
18 treatment. This would exhaust doxycycline's supply
19 prematurely and inappropriately. Further in the
20 study, CDC recommends additional areas of study
21 such as labeling comprehension and simulation
22 studies. We agree with these areas identified and

1 warrant further study for antibiotic medkits.

2 While the extent of inappropriate use was
3 limited in the earlier studies, it's important to
4 note that often studies occur under ideal
5 circumstances in which carefully selected consumers
6 receive detailed instructions. With wider
7 distribution, it's unlikely that all prescribers
8 will maintain the high level of counseling provided
9 in the pilot studies.

10 Adherence to recommended product storage
11 should also be assessed. It's well known that
12 extremes in heat, cold, and moisture can render
13 many medications ineffective. Without proper
14 storage, antibiotics would not only be ineffective,
15 but again promote a false sense of security that
16 can result in behavior leading to increased
17 incidence of the disease that the medication is
18 intended to prevent.

19 Taking antibiotics prematurely or
20 inappropriately, as we have heard today, will lead
21 to resistance. ASHP policy opposes non-
22 prescription status for any medication for which

1 development of resistance is a concern and the
2 society is opposed to non-prescription availability
3 of over-the-counter medkits or their components.
4 However, ASHP would support availability of these
5 drugs without a prescription through mechanisms
6 overseen by public health officials, who would then
7 determine when and where the products are needed,
8 such as community-based caches, including
9 hospitals, health systems, and pharmacies.

10 We encourage the panel to refer to the
11 recent Institute of Medicine study, which we've
12 heard about today, which examines in detail the
13 risks across the continuum of distribution options.

14 Anthrax exposure is likely to be
15 concentrated to a very focused environment,
16 depending on the mechanism of spore distribution
17 and exposure. As an alternative to home
18 stockpiling of medkits, it would be more feasible
19 to design regional and local distribution systems
20 for antibiotics that incorporate appropriate
21 assessment of severity of disease to ensure that
22 procedures and treatment algorithms are followed

1 that produce the most optimized post-exposure
2 therapy.

3 In conclusion, we strongly support and
4 encourage individual preparedness planning and
5 recognize the importance of an all-hazards approach
6 to home readiness. However, ASHP does not support
7 the use of doxycycline medkits for home stockpiling
8 at this time.

9 We look forward to continuing to collaborate
10 with the FDA, CDC, and others on this in other
11 biohazard preparedness plans. Thank you.

12 DR. MOORE: Thank you, Mr. Topoleski.

13 Let's now hear from Ms. Bough.

14 **Association Presentation - Marcie Bough**

15 DR. BOUGH: Good morning. I only have one
16 slide. My name is Marcie Bough. I'm with the
17 American Pharmacists Association, and I serve as
18 our senior director of government affairs. APhA is
19 the largest and oldest established professional
20 society for pharmacists, and we represent over
21 62,000 members, providing care in all practice
22 settings.

1 Thank you for the opportunity to provide
2 comments.

3 APhA supports a step-wise approach for
4 various public health strategies that include
5 exploring the potential feasibility of an
6 FDA-approved medkit containing doxycycline for
7 treatment in response to potential exposure to
8 anthrax. We appreciate that HHS is seeking the
9 advice of the advisory committees on feasibility
10 and the types of consumer studies needed to assess
11 proper use of personal medication kits for a
12 potential home stockpiling.

13 We also appreciate that HHS recognizes the
14 importance and value of outreach to the public,
15 including healthcare organizations and other
16 experts, as more information is gathered, as
17 options are considered, and as lessons are learned
18 from existing programs are shared.

19 From a public health perspective,
20 pharmacists are prepared to serve as responders in
21 the event of anthrax exposure, and educate, and
22 dispense medications in collaborations with local,

1 state, and federal activities for targeted or
2 general use. Pharmacists are often considered the
3 most accessible healthcare provider, particularly
4 in rural areas, inner cities, and other underserved
5 areas with limited access to primary care.

6 As we demonstrated during Hurricane Katrina
7 and other emergency responses, pharmacists serve in
8 a vital role in providing frontline response for
9 clinical services, assessment, education, and
10 dispensing of medications.

11 The successes of pharmacist-administered
12 immunizations in all 50 states, D.C., and Puerto
13 Rico serves as a helpful model for medkits in
14 showing how pharmacists can help improve
15 immunization rates, but also access to a needed
16 medication.

17 As the committees consider the feasibility
18 of home stockpiling of medkits and the types of
19 consumer studies that are needed, APhA recommends
20 you consider the following four key focus areas:

21 One, appropriate and inappropriate use. We
22 are concerned that home medkits may not be used

1 appropriately in the general public, beyond the
2 scope of targeted dispensing. While the intended
3 use, made to improve access, shorten the time for
4 first dose and ease distribution burdens, an
5 informed consumer may be aware that the same
6 medication is also used to treat other medical
7 issues, thereby increasing the potential for
8 inappropriate use of the medication. Such use may
9 also lead to resistance issues and lapses in
10 restocking a medkit with enough doses for first-
11 dose coverage or lengthier treatments for a
12 declared event in an entire household. Product
13 labeling needs to clearly indicate that it's
14 indication only for emergency response.

15 When considering label comprehensions and
16 actual-use studies, we encourage the committees to
17 consider how labeling and educational information
18 on packaging of medkits is understood by the
19 consumers, including information such as
20 directions; indication for emergency response;
21 dosing, including information specific to
22 pediatrics; therapeutic and self-care algorithms;

1 adverse events, interactions, storage, disposal,
2 and other pertinent information.

3 We also recommend that the labeling indicate
4 who would likely be declaring the need for an
5 emergency response medication; for example, the
6 local, state, or other federal health agency that
7 may be communicating the message.

8 Two, storage expiration dates and disposal.
9 Similar to storage with current medications, there
10 is potential for inappropriate storage of home
11 medkits. In the context of emergency response,
12 medications may have lengthy storage times,
13 potentially years in settings that have high
14 temperature and/or humidity fluctuations, thus
15 potentially jeopardizing the integrity and potency
16 of the medication.

17 There is also potential for home medkits to
18 be stored long enough to exceed by years the
19 expiration date. Unfortunately, home storage lacks
20 the benefit of a rotating stock in pharmacies,
21 where storage is more controlled and expiration
22 dates are actively monitored.

1 In addition, our healthcare system is
2 already struggling with the appropriate disposal of
3 medications. Therefore, we encourage the
4 committees to consider the need for strong labeling
5 information related to the appropriate storage and
6 disposal, especially for large stockpiles that may
7 be expired and what to do if you're a local
8 supplier of medication kits or the medication
9 itself. The committee should also consider the
10 potential for take-back programs or exchanges for
11 expired medkits and the costs associated with such
12 activities.

13 Three, equal access and costs. All
14 individuals need to have equal access to receiving
15 a medkit, not just those who have potential
16 insurance coverage or means of cash payment.
17 Payment voucher systems will need to be considered
18 to avoid creating a silo of individuals or
19 underserved, who may not have access to medications
20 or access to a distribution facility in times of
21 emergency response, similar to previous comments.

22 Similarly, any process will also need to

1 consider costs and sustainable business models;
2 specifically, who is paying for the medkits. Is it
3 individuals, families, cash payments, insurance
4 programs, assistance programs, a combination of all
5 that, or a government in combination with any of
6 the state programs, and for what purposes are those
7 said groups paying? For example, is the purpose
8 for preparedness and stockpiling or for actual
9 response and prophylaxis? We recommend the
10 committees consider such issues.

11 Finally, similar to what Dr. James mentioned
12 in his testimony, pharmacies can serve as
13 distribution centers. We encourage the committees
14 to recognize the need for integrating pharmacists
15 and pharmacy locations and infrastructures into
16 whatever the development is for targeted or broad-
17 scale distribution processes for medkits, whether
18 it be by prescription only, a variation of over-
19 the-counter with an intervention, or full over-the-
20 counter, or in combination, depending on the
21 response.

22 Pharmacists can serve to alert, administer,

1 screen, educate, refer, dispense, follow up, and
2 otherwise provide messaging as part of an
3 integrated and overall collaborative response and
4 distribution process.

5 Ultimately, maintaining storage and
6 distribution processes at a pharmacy should be
7 considered as part of a coordinated effort with the
8 local, state, and federal activities for targeted
9 and potential broad-scale scenarios. Pharmacies
10 may also offer flexibility in shipment and supply
11 stock as part of a community response, with an
12 effort to transfer to another response location if
13 needed.

14 Finally, in closing, we need to ensure that
15 consumers are aware of an emergency response and
16 have access to pharmacists and other healthcare
17 providers to provide the important information on
18 appropriate use of these medications as a
19 supplement to product labeling and use algorithms
20 with the packaging.

21 Such activities should not be looked upon
22 solely as distribution of a commodity, but rather

1 as a healthcare interaction. Pharmacists in
2 communities across the country can play an
3 important role in integrating with the emergency
4 response with that community and with how medkits
5 are accessed and dispensed.

6 Thank you for the opportunity and the time,
7 and we look forward to working with FDA and
8 stakeholders on this important issue. Thank you.

9 DR. MOORE: Thank you, Ms. Bough.

10 Dr. Bradley?

11 **Association Presentation - John Bradley**

12 DR. BRADLEY: My name is John Bradley. I'm
13 a pediatrician in infectious diseases at Rady
14 Children's Hospital in San Diego. And my comments
15 today will represent those of the American Academy
16 of Pediatrics. I used to serve on the Anti-
17 Infective Drug Advisory Committee. and I'm still
18 part of the FDA advisor staff, but the comments
19 today are specifically for the Academy of
20 Pediatrics.

21 The academy is a non-profit professional
22 organization of 60,000 primary care pediatricians,

1 pediatric medical subspecialists, and surgical
2 specialists. Disasters are an important part of
3 what the academy does. There's a disaster
4 preparedness advisory council. They are active in
5 the anthrax arena, and there are 28 people who are
6 identified as anthrax experts, although I would say
7 that none of us have actually participated in true
8 anthrax disasters, but we like to model it. We
9 also work very closely with public health
10 authorities.

11 The antibiotics currently approved or
12 recommended by FDA, as have been mentioned, include
13 doxy, cipro, and levofloxacin. And on the FDA
14 website, amoxicillin is also one of the antibiotics
15 recommended, although this is not on the package
16 label.

17 There are a couple of different ways of
18 prepositioning antibiotics. First responders were
19 mentioned earlier, but the FDA had asked our
20 comments to consider a broader perspective, putting
21 antibiotics in the homes of the general population,
22 and I'd like to address those issues. And then

1 there's the issue of prepositioning so that the
2 kits can be prescribed by a pediatrician. Family
3 can get the prescriptions from the pediatrician,
4 who can then explain risks, benefits of the kit,
5 when not to use it, what sort of side effects to
6 expect.

7 Then there's the issue that was brought up
8 by Homeland Security, where if the cloud should
9 appear over a city and the goal is to get
10 antibiotics to the population within 48 to
11 72 hours, that some of the modeling that was done
12 in the mid to late 2000s included having the postal
13 service actually deliver antibiotics to the home.

14 So this is sort of a push deployment rather
15 than prepositioning, but the issues about how
16 parents will reconstitute tablets and the
17 formulations of doxycycline that would be
18 appropriate for that kind of deployment, as opposed
19 to sitting down comfortably with your physician and
20 discussing the risks and benefits, are two
21 completely different issues.

22 So children grow. There is a lot of

1 evidence base for that. And so whatever discussion
2 occurs between the physician and the family at the
3 time that the kit is dispensed, the kids will get
4 bigger. The parent and provider needs to know the
5 weight of each child at the time of dosing. And
6 for those of you with infants and school-aged kids,
7 I challenge you to write down the weights of all of
8 your children, especially the dads, because we
9 usually don't know that sort of information.

10 So it requires that a weight scale be
11 present in each home, a functioning weight scale,
12 which may not be the case. And the emergency
13 medicine community has a way to very roughly dose
14 children based on size, which is a little bit
15 easier to calculate. Again, a rough measurement,
16 this would be done in the event there's no scale
17 present.

18 The suspension, the discussions earlier,
19 there is a suspension of doxycycline. And I would
20 say it's easier for a parent to just put liquid
21 water in a suspension bottle, shake it up, and
22 measure as opposed to the beautiful directions in

1 the postal model, where you put the tablets in the
2 bowl, let it sit for five minutes, crush it, add
3 your food.

4 So for prepositioning, where suspension and
5 volume and expense perhaps are not such huge
6 issues, I think suspension should be considered for
7 prepositioning. On the other hand, after an
8 exposure to get drug out to the families as quickly
9 as possible, we're loading up all those postal mail
10 trucks with doxycycline. To have the smallest
11 weight and volumes for the trucks would be
12 important. And the Strategic National Stockpile
13 has told us that they will only stockpile a certain
14 amount of suspension because the tablets are far
15 easier for them to manage.

16 I didn't get the briefing materials until
17 after I turned in my slides, so my comments about
18 the suspension go beyond what has been discussed
19 earlier today about the tablet formulations.

20 Also, the families expand, and in the
21 Minnesota experience, there was a change in family
22 composition that they documented each year, that

1 ranged between 5 and 10 percent. And Dr. James was
2 saying, well, between the time you get the kit and
3 when you dispense it, you may not have children at
4 home. But my view is you'll have more children at
5 home. Babies will be born. And maybe in southern
6 California, there would be an even greater change
7 in the family composition each year.

8 So we need to take into account, after you
9 dispense it, some way to keep in touch with these
10 families annually or whatever in order to update
11 their kits to make sure that they've got exactly
12 what they need. We don't want them shortchanging
13 older kids by giving some of their supplies to the
14 new infants.

15 I'm going to just breeze through these since
16 everyone else has already talked about them.
17 Directions should be clear. Health literacy and
18 language barriers need to be addressed. Care
19 providers need to know how to store the medicines,
20 monitor expiration dates, blah, blah, blah.

21 Communication. How is the information, that
22 they're supposed to take their medicines, get out?

1 And Dr. Neely here mentioned Facebook. In many of
2 the families, the teenagers will probably find out
3 that there's going to be an event before the
4 parents do.

5 Parents need to be informed about the
6 safety, side effects. And during an event, if the
7 kids take doxycycline and have some sort of adverse
8 event, we need to figure out how they can get
9 medical advice to stop the drug if there's a
10 reaction and start another effective post-exposure
11 prophylaxis drug. And the others have been
12 addressed.

13 Also, if a drug is prepositioned in the
14 general population, there are a lot of families
15 that take care of disabled kids, who are on
16 multiple meds. And in these medically fragile
17 families, there may well be drug-drug interactions
18 with doxycycline, and the parents need to be
19 informed of those sorts of issues.

20 Doxy is associated with staining of teeth.
21 That's not a big deal when there's a 40 percent
22 mortality of inhalational anthrax. So I don't want

1 to make any issue there. We believe a little bit
2 of teeth staining and survival, certainly, the
3 benefits outweigh the risks. However, we all know
4 that you can't take tetracycline with calcium-
5 containing products because there's a 50 percent
6 decrease in absorption. However, with doxy,
7 there's a 20 percent decrease in absorption.

8 If you look at package labels for acne, it's
9 a little less absorbed, but it shouldn't be a
10 problem. For acne, that may be okay, but when
11 we're talking about anthrax post-exposure
12 prophylaxis in a life-or-death situation, where
13 exposure is everything, that 20 percent may make a
14 difference with some kids.

15 These studies were done in the '70s. These
16 studies were done 40 years ago. And I think that
17 we need to do up-to-date current studies with
18 current technology so that we can know that these
19 drugs are actually absorbed using diets that
20 families use, the infants drinking milk, teenagers
21 eating pizza. So I think that there's some need
22 for redoing some of the pharmacokinetic and

1 pharmacodynamic studies.

2 Equal access was already mentioned. Who
3 pays for the kit? We want to make sure everyone
4 can get it. Schools, being a place where some of
5 these drugs may be dispensed; working through
6 public health authorities as we did with flu
7 vaccine; and again, working very, very closely with
8 public health departments and the FDA.

9 So, in summary, I think that the planning
10 that's all going on, Dr. Korch mentioned PHEMCE,
11 and the agency, I think all working together, we
12 could be prepared to address the cloud when and if
13 it should arrive. Thank you very much.

14 **Questions and Clarifications**

15 DR. MOORE: Thank you, Dr. Bradley.

16 We're significantly over time. I'll
17 entertain a few questions and clarifications before
18 we break for lunch.

19 Yes. Dr. Hilton?

20 DR. HILTON: I haven't heard anyone mention
21 the possibility of a barrier method like a mask.
22 And I feel like a society that can create the

1 magical things that we create should surely be able
2 to create that.

3 Secondly, I would also like to mention that
4 we have talked about distribution and retrieval of
5 these kits, but I feel like there's been inadequate
6 attention to neutralization of the drug and
7 disposal of even the waste products that come along
8 with it. I'd like to contrast this receptacle
9 with, say, a sugar packet. I mean, does it really
10 have to be this substantial?

11 Finally, we are reacting -- our society is
12 reacting, to two terrorist events, the anthrax and
13 the World Trade Center airline crashes, and putting
14 huge changes into place like through security at
15 airports, and now this reaction. And I just wonder
16 is anthrax so unique that the next attack will be
17 just something very different? Should we really be
18 spending so much attention on anthrax? Thank you.

19 DR. MOORE: Thank you. Dr. Parker?

20 DR. PARKER: We heard from the AMA, and I
21 just wanted to see if I was missing anything from
22 anyone else. What do we know about anthrax in a

1 pediatric population versus an adult population?

2 DR. NEILL: I can make one comment to that.
3 I see in a government review that was impaneled in
4 2006, a single reported cases of inhalational
5 anthrax -- I beg your pardon -- two reported case
6 of inhalational anthrax in the reported medical
7 literature.

8 DR. PARKER: In a pediatric --

9 DR. NEILL: In a child.

10 DR. MOORE: Thank you, Dr. Neill.

11 I will defer to my other pediatric
12 infectious disease colleagues about that. Any
13 other -- no? Okay. Well, I have no idea.

14 Dr. Reidenberg?

15 DR. REIDENBERG: Yes. Two questions. Does
16 anybody know if degraded doxy will produce the
17 Fanconi syndrome the way degraded tetracycline and
18 the older tetracyclines do? And my second question
19 is, do we know what the risk of developing
20 Clostridium difficile infection is in people who
21 take doxycycline even for just 10 days?

22 DR. MOORE: I'll say that the risk with

1 any -- I'm not sure that there are any
2 data -- well, I take that back. Speaking about
3 doxycycline and the risk of C. diff, there have
4 been associations. But in terms of the actual
5 risk, the question that's posed is like a Zen
6 riddle. What's the sound of one hand clapping? It
7 can't be assessed with current data.

8 About the Fanconi syndrome, any takers? No?
9 All right.

10 Let me do this -- I'm sorry?

11 DR. GORMAN: About the Fanconi
12 syndrome -- I'm Sue Gorman from CDC -- I believe it
13 does not cause Fanconi syndrome once it's degraded.
14 There is some literature from the '70s that says
15 that there was a formulation change that prevented
16 that from occurring. So the answer to that is no.

17 DR. MOORE: Excellent. Thank you very much.

18 We're going to take one more question,
19 Dr. Young, and then we'll go to lunch.

20 Ms. Young. Sorry.

21 MS. YOUNG: Yes. I'm wondering in terms of
22 the overall framework. This is a counter-terrorist

1 and a defense measure. While we've heard that the
2 assumption is not proven, the assumption that this
3 kind of countermeasure among first responders will
4 incentivize them. So I'd like to see more about
5 that.

6 But I guess one of my questions is, if we
7 accept this as a countermeasure for our country and
8 it goes step-wise into broader application, what
9 about other countries, and the fact that the whole
10 globe might be covered with these antibiotics kits
11 and the potential for misuse and such?

12 So that's one concern.

13 Then my other big concern is I wondered if
14 the defense agencies have really considered the
15 bioengineering impact of an agent that really would
16 be able to counter whatever we do put in the kits
17 and the potential for chaos that that could create
18 in the public's mind of being equipped with
19 something that's supposed to work and it really
20 doesn't.

21 So those are my concerns.

22 DR. MOORE: Thank you very much.

1 We will now break for lunch. We will
2 reconvene again in this room in one hour from now,
3 which will be 1:15. Please take any personal
4 belongings you may want with you at this time.

5 Committee members, please remember that
6 there should be no discussion of the meeting during
7 lunch, amongst yourselves, with the press, or with
8 any member of the audience. Thank you.

9 (Whereupon, at 12:16 p.m., a luncheon recess
10 was taken.)

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A F T E R N O O N S E S S I O N

(1:14 p.m.)

Open Public Hearing

DR. MOORE: It's 1:15. We'll go ahead and get started with the afternoon session. So we're going to start with the open public hearing.

Both the Food and Drug Administration and the public believe in a transparent process for information gathering and decision making. To ensure such transparency of the open public hearing session of the advisory committee meeting, FDA believes it is important to understand the context of an individual's presentation.

For this reason, FDA encourages you, the open public hearing speaker, at the beginning of your written or oral statement to advise the committee of any financial relationship that you may have with any company or any group that is likely to be impacted by the topic of this meeting. For example, the financial information may include a company's or a group's payment of your travel, lodging, or other expenses in connection with your

1 attendance at the meeting.

2 Likewise, the FDA encourages you, at the
3 beginning of your statement, to advise the
4 committee if you do not have any such financial
5 relationships. If you choose not to address this
6 issue of financial relationships at the beginning
7 of your statement, it will not preclude you from
8 speaking.

9 The FDA and this committee place great
10 importance in the open public hearing process. The
11 insights and comments provided can help the agency
12 and this committee in their consideration of the
13 issues before them. That said, in many instances
14 and for many topics, there will be a variety of
15 opinions.

16 One of our goals today is for this open
17 public hearing to be conducted in a fair and open
18 way, where every participant is listened to
19 carefully, and treated with dignity, courtesy, and
20 respect. Therefore, please speak only when
21 recognized by the chair. Thank you for your
22 cooperation.

1 With that, we will go to speaker number 1.

2 MR. TAN: Thank you, Mr. Chairman. Good
3 afternoon. My name is Lawrence Tan. I'm the chief
4 of emergency medical services for Newcastle County,
5 Delaware. And in the interests of public
6 disclosure, I have no financial arrangements with
7 any of the companies that would be benefitted or
8 impacted by this hearing.

9 I'm representing the Emergency Services
10 Coalition for Medical Preparedness in addition to
11 the EMS community as both an EMS chief and past
12 president of the International Association of EMS
13 Chiefs.

14 The coalition was formed to lead the
15 development of a national strategy to protect
16 providers in the event of a large-scale biological
17 attack. The coalition has drawn support from the
18 major emergency services associations, which
19 represent more than three million responders.

20 The coalition urges you to proceed with all
21 speed and diligence to protect our people, their
22 families, households, and agencies with deployment

1 of medkits to the emergency services sector. By
2 protecting emergency services responders, you'll be
3 protecting a critical component of the local
4 infrastructure.

5 We acknowledge the potential risks of
6 inappropriate use of antibiotics, but feel
7 confident that our membership understands the
8 importance of using such medicines appropriately
9 for the intended purpose and specific indications.
10 Home medkits should be an essential part of our
11 equipment and provide our personnel the confidence
12 to focus on the needs of our communities during a
13 catastrophic event, knowing that their families are
14 protected.

15 A comprehensive study of the factors
16 affecting a responder's willingness and ability to
17 report for duty has cited that, one, family safety
18 and support, two, an increased attention to
19 employee safety, and, three, increased focus on job
20 expectations as keys to emergency services
21 providers being able to fulfill their duties during
22 a major emergency. Medkits placed in the workplace

1 and responder homes can address each of these
2 areas.

3 Emergency services personnel routinely
4 handle equipment and materials that are far more
5 lethal and have more profound consequences than the
6 antibiotics that would be included in the medkits.
7 Some responders carry guns and are authorized to
8 use lethal force in the performance of their
9 duties. Others administer medications, including
10 scheduled drugs, to critically ill patients outside
11 of the hospital. And yet others work with
12 hazardous materials in lethal environments under
13 life-threatening situations. All may potentially
14 enter operational areas during the performance of
15 their duties that could result in exposure to
16 biologic hazards.

17 We've been given this responsibility because
18 we're trained and routinely demonstrate our
19 self-discipline and ability to follow instructions
20 and protocols.

21 A widespread anthrax attack on this nation
22 will have consequences unlike anything that we've

1 seen before. The potential for civil disruption is
2 great. And unlike other scenarios, the homes and
3 families of our responders will be affected as
4 well. The nation will expect emergency services to
5 function throughout the attack and its aftermath.
6 We can ill afford to have our personnel diverted by
7 the very natural inclination to ensure the safety
8 of their families.

9 Ladies and gentlemen, thank you for your
10 time and attention. And on behalf of the
11 coalition, I urge you to proceed with the
12 comprehensive study on home medkits for emergency
13 services, confident that we have sufficient
14 justification, knowledge, and oversight of our
15 personnel and organizations for such a program. In
16 doing so, you'll be protecting the protectors and a
17 component of the vital infrastructure of this
18 nation.

19 DR. MOORE: Thank you very much. We'll move
20 onto speaker number 2.

21 DR. MINSON: I don't have a PowerPoint.

22 Thank you very much. My name is Matt

1 Minson. I'm the medical director for Superior
2 Energy Services. They paid for my travel and are
3 viewing this as part of their good corporate
4 citizenship.

5 We're a corporation that provides, among
6 other things, the preeminent global response
7 capability for well-controlled emergencies in
8 upstream energy sector fire-fighting. As medical
9 director, I have the responsibility for the
10 occupational health system oversight, as well as
11 the operational emergency medical support, and our
12 surveillance programs post-incident.

13 Outside my position with Superior, I'm the
14 medical director for one of the federal urban
15 search and rescue teams, Texas Task Force 1. I'm
16 also a member of the National Fire Protection
17 Association's technical committee advising homeland
18 security issues relative to first responder
19 protections, and weapons of mass destruction, and
20 hazardous materials, and environments.

21 Finally, I'm a member of the National
22 Sheriff's Association's homeland security

1 committee. It's at their encouragement that I am
2 doing this presentation, to talk about our clinical
3 enterprise for the global response teams.

4 Because of the clinical austerity of the
5 work environment, the potential for a transition
6 from one theater of activity back to another
7 without return to home base, and because of
8 documented situations in which we've had
9 individuals who have had a diagnosed medical issue,
10 specifically an infectious disease issue, receiving
11 medication that did not have climate and expiration
12 integrity, we've outfitted some of the personnel in
13 those teams with individual caches of materials,
14 specifically antimicrobials along with
15 antimalarials. We've done vaccination programs as
16 well to protect them.

17 I really want to talk specifically about the
18 antimicrobials. I think what's interesting is
19 we've accrued over 4 million manhours and have had
20 only one incident that was clerical in nature and
21 no clinical incidents.

22 So as far as the take-away for that in this

1 group, I'd offer, really -- there's two pieces.
2 From the practice perspective, an FDA-approved
3 product provides consistency, structure, and
4 advocacy for the clinician. And in all fairness, I
5 think it's important to remember that we would
6 prefer to have a clinically driven, prescription-
7 approved, and clinically overseen program so that
8 any altered event could be recorded. Thank you.

9 DR. MOORE: Thank you very much.

10 Speaker number 3?

11 MR. WILLIAMS: Thank you, Mr. Chairman. My
12 name is Wayne Williams. I am a consultant
13 representing Sharps Compliance, Inc. They did pay
14 for my travel here, and I do have a financial bond
15 with Sharps Compliance, Inc. as a consultant.

16 Sharps would like to just take the
17 opportunity -- and originally we were going to run
18 through these slides, but most of these slides have
19 been covered throughout the discussions earlier
20 today. But Sharps Compliance, Inc. is an
21 organization that works on basically the
22 safekeeping and removal of waste byproduct. And

1 because of my background with the government, I
2 approached them in looking at the medkit process.
3 One of the areas that I approached them at is
4 actually the backend, which was discussed with
5 several folks in how is it stored; how do we get it
6 out once it's got expiration date, or is expired,
7 or has been recalled. And that is one of the areas
8 where Sharps has accelerated in the commercial
9 industry with its takeaway process.

10 So we approached it in that manner, versus
11 the actual use of the doxycycline, which is a
12 licensed drug for the use of Bacillus anthracis.
13 So in the process of making the medkit, if
14 approved, our approach would be to help the
15 industry both on the drug side of the house and the
16 government in some of the technologies and
17 capabilities of properly storing the product while
18 it's at the home or at the first-responder level,
19 also in the tracing and trackability of that
20 product, whether it be with the manufacturer of the
21 drug or the needs of the government in
22 understanding where it's at and when it's being

1 used. And then finally, when the product is
2 determined that it is no longer functional or in
3 use, actually recovering that through a process
4 called the RX TakeAway, which is a licensed product
5 to recover antibiotics and pharmaceuticals through
6 the U.S. post office, where it is properly disposed
7 of.

8 It is actually not destroyed, but it is
9 repurposed. It is an environmentally green
10 approach, where the product would then be used in
11 environmentally friendly byproducts. It is
12 currently being used in the retail side of the
13 house for the recovery of drugs at this point
14 already.

15 So that was basically our approach in
16 reference to the medkit process, basically doing a
17 collaboration with industry, taking the licensed
18 drug, building it within the kit where you would
19 have this recovery capability, and not only with
20 the actual movement of the product, but then the
21 tracer side of the house, which is also a licensed
22 application where you're able to trace this data

1 that is required: what individual, what household
2 has this product, what is the lot number, the
3 expiration date. And so then the individuals can
4 either reach out via electronic means that your
5 medkit is due to expire, be recovered maybe back
6 through the manufacturer of the drug, where
7 incentives can be given for return of that product.
8 That way we're not leaving this product out there
9 in reference to the different medkit processes.

10 Thank you.

11 **Charge to the Committee and Discussion**

12 DR. MOORE: Thank you very much to the
13 speakers.

14 The open public hearing portion of this
15 meeting is now concluded, and we will no longer
16 take comments from the audience. The committee
17 will now turn its attention to address the task at
18 hand, the careful consideration of the data before
19 the committee as well as the public comments.

20 So we'll proceed to the charge to the
21 committee.

22 Dr. Cox. Dr. Laessig?

1 DR. LAESSIG: So we've heard many excellent
2 presentations and discussion this morning that have
3 raised lots of important issues regarding
4 doxycycline medkits. and we greatly appreciate the
5 participation of all stakeholders and committee
6 members in today's meeting, and everyone's valuable
7 perspective and expertise.

8 So as Dr. Moore has just mentioned, at this
9 time we ask the committee to turn its attention to
10 the questions. And you'll note that although the
11 questions were not written specifically focusing on
12 medkits for first responders, we invite you to
13 respond to the questions with this population in
14 mind, as well as the general population.

15 So looking at question number 1, this is a
16 discussion question, and we ask that you please
17 comment on the public health implications of a
18 prescription doxycycline medkit intended for post-
19 exposure prophylaxis for an anthrax
20 counterterrorism event. Specifically, please
21 address potential benefits and risks if a
22 prescription medkit were approved with the

1 intention of home storage.

2 So looking at question 2, this is actually a
3 two-part question; part A, please comment on
4 additions or modifications to the proposed and/or
5 completed studies, ergo, the label comprehension,
6 palatability, simulated use, or additional studies
7 that would help to assess the risks and benefits.
8 What types of additional studies might be helpful
9 to assess how users would behave in a real-life
10 situation?

11 Part B, what is a reasonable percentage of
12 study subjects who should understand the various
13 components of the label and/or be able to refrain
14 from using the product for other uses?

15 Question number 3, another discussion
16 question, the doxycycline medkit proposal includes
17 instructions for dosing children and adults who
18 cannot swallow pills using the 100-milligram
19 tablets. Please comment on any additional
20 recommended studies to evaluate these dosing
21 instructions in this population.

22 Lastly, question 4, the final discussion

1 question, doxycycline is available in other dosages
2 and as a liquid formulation. Please discuss the
3 pros and cons of the home preparation mixture
4 versus other available formulations for use in a
5 medkit.

6 Back to you, Dr. Moore.

7 DR. MOORE: Thanks, Dr. Laessig.

8 So before we have open discussion around the
9 committee, I want to make sure everybody -- I
10 passed over a lot of questions in the morning, so
11 I'd like to discuss those or everybody have a
12 chance to ask their questions before we have open
13 discussion.

14 Dr. Day was next on the list.

15 DR. DAY: Thank you. I appreciate that.

16 The idea to only use this under an emergency
17 is coming across in a lot of the materials, and we
18 saw that on the bag that was passed around today
19 for the medkit. And there is so much emphasis on
20 emergency and not on emergency for what. And
21 there's only one little tiny mention of anthrax way
22 down at the end of one of the three or four

1 paragraphs on the bag.

2 So that can be a problem. First of all,
3 people not knowing what kind of emergency, and then
4 having it in a blizzard, taking it when there's a
5 blizzard, and so forth, and then not rereading
6 carefully. But also, there have been other medkits
7 under consideration, such as the one for pandemic
8 flu was mentioned this morning, with the use of
9 Tamiflu and so on.

10 So this generic title which says Household,
11 da-da-da, for Antibiotics is pretty generic. And I
12 was wondering if the people who have been designing
13 and doing these studies have taken this into
14 account, and whether it ought to be specified
15 specifically for what the indication is because,
16 after all, the actual medication -- even if it were
17 the same medication, the dosing would be different
18 for different indications.

19 DR. MOORE: Thank you.

20 Dr. Landis?

21 MS. LANDIS: My comments mostly were on
22 point number 3 or question number 3. Do you want

1 me to defer to that point?

2 DR. MOORE: It's up to you, Ms. Landis.

3 MS. LANDIS: Mine goes back to question 3,
4 talking about instructions for dosing adults and
5 children who are unable to swallow medications, and
6 I don't know if that can be answered.

7 My biggest question was, there's a lot of
8 steps that are put into the directions that they
9 have there. Was there any consideration given to
10 having a complete package that would either have a
11 pill crusher added, which is a very inexpensive
12 device, and an empty bottle that would have a line
13 so that people could just fill it up -- I guess
14 what I'm trying to say is they shouldn't have to go
15 through their house finding bowls and other things.
16 It should be a complete kit, ready to go with the
17 flavoring if necessary.

18 Were any of those pieces put in place when
19 they put this medkit together? I don't know if
20 anybody can answer.

21 DR. MOORE: Does anybody from HSA have a
22 response?

1 DR. YESKEY: I think right now that, no, we
2 didn't consider that. It's not that we wouldn't
3 ever consider something of making a complete kit,
4 so your suggestions are welcomed and comments are
5 welcomed with that regard.

6 DR. MOORE: Good point. Dr. Woods?

7 Yes. I'm sorry. Please go ahead.

8 DR. METZ: So the design that we currently
9 have and what was passed around has been modified
10 to some degree from the original kit that was
11 released in the CDC study. But we acknowledge that
12 there's still a lot of potential improvements to be
13 made, keeping in mind of course the complexity of
14 the kit will increase the cost and potential
15 barriers to people purchasing it. The more pieces
16 that are inside, not only does it get more
17 expensive, but it gets larger and more difficult to
18 package and distribute. But these are all issues
19 that I think are worth looking at in depth.

20 MS. LANDIS: And I would challenge, when
21 they look at the medkits, to maybe identify what is
22 more important. Maybe adding that extra dollar or

1 two to be sure that patients are compliant and
2 getting the correct dosage versus having to kind of
3 look around and find all those pieces that are
4 necessary. I think you would probably find most
5 parents would opt to pay that extra dollar or two
6 to be sure that it's easy and they're going to get
7 the correct dosage, so maybe a study.

8 DR. MOORE: Sounds fine.

9 Dr. Woods?

10 DR. WOODS: Thanks. I'd like to follow up
11 on a line of thinking that, actually, Dr. Kaplan
12 started, and then Mr. Blumenstock actually
13 triggered even some more thoughts along this line.
14 But it has to do with the ultimate distribution
15 system that we use for this product: is it going
16 to be available to the general public, restricted
17 only to first providers? And if it's only
18 restricted to first providers, how do we really
19 know that?

20 One of the things we do know, though, from
21 past experience with previous anthrax scares was we
22 created serious drug shortages in particular with

1 cipro. And I guess, as I think about the
2 availability of a product of this nature, when the
3 general public becomes aware of that, do we create
4 some kind of mass hysteria that leads to additional
5 drug shortages? And has anyone done any
6 forecasting based on past history to figure out
7 whether or not the pharmaceutical supply chain
8 would be equipped to handle something like this?

9 So that would be my first question. Has
10 anybody really thought that through, especially
11 given the fact that these are drugs that we have
12 intermittent drug shortages with already?

13 DR. MOORE: Excellent point.

14 Is there anybody available to respond from
15 the sponsor?

16 DR. GORMAN: Sue Gorman, CDC. I don't
17 believe that we have experienced any shortages of
18 doxy and cipro oral tablets thus far in our
19 stockpiling endeavors. Periodically, there might
20 be something coming up, but we stage our
21 procurements so that we don't create a market
22 shortage, where we don't want to interfere with the

1 regular supply chain, so we haven't had that issue.

2 DR. WOODS: To this point, if we were to
3 create a product like this, we haven't done any
4 forecasting based on what's happened in the past.

5 My second question relates to who will
6 actually pay for this, whether it's the employee,
7 the employer. And then once it's returned, how
8 does that work? Is the employee on the hook to
9 again pay for another packet?

10 I think we saw that the predicted price was
11 in the \$20-some range. And if you're talking about
12 first responders and their families, are they on
13 the hook for 100 bucks? I think there are some
14 economic issues that really need to be thought
15 through.

16 My final question -- and again, not to focus
17 on the drug shortage issue, but it seems to be
18 something that is just with us every single day in
19 practice.

20 Do we have any idea whether we have enough
21 anti-anthrax antibiotics in the cache and then
22 available just for general practice should we see a

1 run? And I don't know who, again, would do that
2 forecasting, but I just wonder about dire
3 circumstances and the availability of these
4 products for their other indications.

5 DR. MOORE: Again, I'll look to someone from
6 Homeland Security or other sponsors.

7 DR. GORMAN: Regarding whether we have
8 enough oral antibiotics right now in the Strategic
9 National Stockpile to cover the goal, the answer is
10 yes. We have enough to cover the goal that's been
11 defined by Homeland Security for the amount of
12 people that we need to be prepared for.

13 So we are covered right now, so any
14 additional procurements that were made right now
15 would not impact that. We actually have more than
16 enough than we need to cover the goal for persons
17 for anthrax for post-exposure prophylaxis right now
18 in the stockpile.

19 DR. WOODS: Can you guys tell us what that
20 goal is without having to kill us?

21 [Laughter.]

22 DR. KORCH: It's in the range of tens of

1 millions, without giving any specific number. We
2 didn't put it up on the website. I think, for the
3 most part, it's built upon requirements that were
4 derived from a variety of modeling studies.

5 So the whole process of requirements
6 building relates to our relationship with DHS in
7 terms of developing realistic scenarios. And from
8 there, we then use our BARDA modeling capability to
9 look at the public health impacts, looking at the
10 affected populations, looking at what the dimension
11 of need would be, and from there deriving a
12 coverage factor for multiple events.

13 So it's in the tens of millions and that's
14 what I can say.

15 DR. MOORE: Thank you. As a bit of
16 housekeeping, let me remind the speakers -- thank
17 you very much for your response. I would actually
18 remind the speakers to introduce yourselves again.

19 DR. KORCH: I'm sorry. George Korch from
20 HHS.

21 DR. MOORE: Thank you.

22 DR. KORCH: That's tens of millions of

1 treatment courses, so with a 60-day supply being
2 the full course.

3 DR. MOORE: Dr. Ockenhouse?

4 DR. OCKENHOUSE: Yes. Thank you very much.
5 I would like to address my question to Dr. Korch.

6 George, what's the scientific or medical
7 rationale for provides post-exposure prophylaxis to
8 family members? And this is distinct from first
9 responders. And how does that gel with the natural
10 history of anthrax?

11 DR. KORCH: Well, the natural history of
12 anthrax, of course, relates primarily to exposure
13 to agricultural products. And so the history that
14 we have at this point doesn't really take into
15 account, except under very unusual circumstances,
16 the development of an aerosolized material. I
17 mean, that has happened. We have seen it in small
18 outbreaks, generally associated with hides or
19 misuse of materials. But for the most part, a
20 natural course would be from a gastrointestinal.

21 I don't know if, Chris, if I'm --

22 DR. OCKENHOUSE: No, no. I'm sorry, George.

1 I probably phrased my question inappropriately.

2 The question is, what is the risk to family
3 members from first responders who may have been
4 exposed to an aerosolized attack?

5 DR. KORCH: Well, our assumption is that a
6 wide community, an entire community, as in a large
7 city or a large geographical area, is
8 simultaneously exposed. There's no differentiation
9 in terms of segment of a population that does or
10 doesn't have a specific possibility in that
11 downwind cloud or downwind event. And so the
12 presumption being, if individuals have a
13 probability as a function of how close they are to
14 the initial release -- that there is an idea or
15 assumption about what an ID50 might look
16 like -- then we would consider all populations
17 downwind of that to a certain degree to have been
18 exposed.

19 So the rationale in terms of scientific
20 rationale for children of first responders versus
21 children of anybody else, there's no specific
22 scientific rationale there. But as you heard from

1 the representative from the EMS communities and in
2 my comments as well, one of the principal aspects
3 of the proposed methodology for this population of
4 first responders is to create, at least for that
5 sector of our communities, a peace of mind or an
6 ability for relatively rapid capability for
7 treating -- or for post-exposure, prophylaxing the
8 family members.

9 I don't know if that addresses your --

10 DR. OCKENHOUSE: Well, if the indication is
11 for a mass biologic attack, then first responders
12 aren't going to be the only ones attacked. And we
13 should be then talking about providing medkits for
14 the population. It is a more likely scenario, just
15 like we saw down at Congress or the postal office,
16 that first responders will respond to a very
17 localized attack of anthrax. And in that scenario,
18 should family members be provided medkits?

19 DR. KORCH: There has been discussion in the
20 past of a general distribution or a general
21 availability of a medkit to the populations. And I
22 think you've heard responses related to the

1 targeting or the applicability relative to other
2 mechanisms that we have in play, those being the
3 national federal stockpile maintained by the CDC
4 and capable of being delivered, if I'm
5 understanding, if I recall the statistics, within a
6 12-hour notification.

7 DR. GORMAN: Or sooner.

8 DR. KORCH: I'm sorry? Or sooner,
9 depending. So within a 12-hour period, anywhere in
10 the country, those materials can be made available
11 then to the state and local jurisdictions according
12 to plans at those localities for setting up points
13 of distribution and effectively providing this in a
14 timely fashion to the rest of the population.

15 So notwithstanding these medical kits that
16 have been described here, that is the concept of
17 operation for anywhere in the country, regardless
18 of what sector of the population you find yourself.

19 In addition to that, there are other
20 components that localities choose with regard to
21 caches of material that are much more forward for,
22 again, specific segments of the population.

1 So we see this medkit option for forward
2 deployment in homes for the first responder
3 community to be an augmentation to currently-
4 existing capabilities that the nation is building.

5 DR. MOORE: Thank you. I think it's safe to
6 assume that if the first responder is taking it,
7 everybody in the family is going to be taking it,
8 if it's a mass attack rate. The secondary attack
9 rate from one individual to another with anthrax is
10 non-existent. The issue is being available.

11 DR. KORCH: Yes.

12 DR. MOORE: But all that scientific data,
13 that knowledge, I'm sure will go out the window in
14 a real situation. When you have the firemen taking
15 the antibiotic, I'm sure that the kids will get it,
16 too, if I understood you correctly.

17 DR. KORCH: That's the assumption. Yes.

18 DR. MOORE: Reasonable.

19 Dr. Rogers had a question. Sorry.

20 Ms. Rogers, you had a question.

21 DR. ROGERS: I have a question for the
22 doctor, George. A couple of things, when you were

1 talking about your studies, California, Texas, New
2 Mexico, Arizona, Michigan have a high population of
3 Latinos. Some of them may be first responders.
4 Their spouses and their family may not speak
5 English.

6 So is this going to be translated into
7 Spanish or has it been translated into Spanish?

8 DR. KORCH: I'm not familiar with how the
9 postal service, either the current distribution or
10 the future deployments to various localities,
11 whether it will or not. So in terms of current
12 practice, I refer to Dr. Yeskey. I don't
13 believe --

14 Has this been translated at this point? And
15 that's not probably the only population of interest
16 with regard to foreign speaking.

17 DR. ROGERS: Right.

18 DR. METZ: Sorry. I didn't introduce myself
19 last time. Matthew Metz from BARDA. And I think
20 an important point to keep in mind here is we're
21 not done working on the design of this. And so I
22 think it would be premature to begin translation of

1 it because it's changed since the CDC study. And I
2 think based on what we learn today, it may be
3 likely to change again, as well as from the
4 clinical studies that we have ongoing right now to
5 look at things such as label comprehension.

6 But that would ultimately I think be a very
7 relevant concern and something that BARDA and HHS
8 would certainly attend to, the importance of making
9 sure that it's in appropriate languages if it's
10 ultimately produced and distributed.

11 DR. KORCH: The question and instructions
12 already have been translated into Spanish. So to
13 follow Matt's point, again, I think the
14 recommendations of this body are very important to
15 consider. And certainly, in terms of
16 comprehension, we don't want the fact that somebody
17 doesn't understand English to be the barrier to
18 comprehension of the label.

19 DR. ROGERS: Let me ask this second
20 question. And that is, has this been tested with
21 minority populations or only the majority
22 population?

1 DR. KORCH: Minority as a function of
2 different language groups or racial groups?

3 DR. ROGERS: Any minorities, minorities in
4 general.

5 DR. KORCH: I think the information that was
6 presented earlier from the CDC did represent, in
7 the St. Louis study, a cross-section of that
8 community to include African-American populations.
9 I don't know if the other individuals from CDC, but
10 certainly with regard to the comprehension studies
11 that are currently ongoing, for which recruitment
12 is happening, it will be important, as I mentioned,
13 to look at cross-sections of the community where we
14 will be enrolling. And to that extent, having not
15 just educational level but a good representation
16 from across the various ethnic and racial groups is
17 going to be important as well for gathering
18 information on the general applicability of both
19 comprehension, use, all of the other human factors
20 that really need to be addressed in this particular
21 context.

22 So yes. We envision the need to be sure

1 that we have good representation as it reflects
2 both the first responder community and other
3 members because other family members will not be
4 the first responders themselves.

5 So does that help answer the question?

6 DR. ROGERS: It answers part of the
7 question, to not linger on it. Thirdly, I will go
8 with what Dr. Wolfe had previously mentioned in
9 terms of cost and someone else, one of my other
10 colleagues over here, in terms of cost, that when
11 you look at some families, in particular in the
12 minority population, there may be two generations
13 of families living together, which means it's a
14 high -- that they're more than a family of five.
15 It could be a larger family of which they are
16 living together.

17 I'm very concerned that if they're going to
18 have to pay 20 bucks for each one of the family
19 members there, this could be quite costly. I'm not
20 sure if you're aware of the fact that deputy
21 sheriffs, who are first responders, don't make a
22 lot of money.

1 DR. KORCH: Understood. And again, the idea
2 here is to provide yet another level or layer for
3 the possibility of protecting these populations,
4 this particular group. We don't know what the
5 price point is going to be. I mean, people are
6 using a number right now. But we haven't had
7 discussions. And partially, what we're asking this
8 advisory board is for us, in terms of moving
9 forward with recommendations on how we should be
10 evaluating and looking at this. Equity is a
11 concern, not just for this particular concept that
12 we're looking at.

13 We ask in our general communities for a wide
14 range of things for preparing families against a
15 variety of emergencies. This is just one component
16 of a number of things that we've asked that
17 individuals and families assume as part of their
18 own personal preparation.

19 So I don't discount the fact that there is a
20 cost associated, that there would need to be
21 hopefully a price point that allows for or doesn't
22 disallow, in a major way, a disincentive for doing

1 this. But by the same token, there are certain
2 opportunities that I think -- across this
3 particular community that we're talking about,
4 advantages that they would see that would argue
5 strongly for the opportunity to be able to have
6 this as a method of protection for themselves and
7 their families.

8 DR. MOORE: Thank you. Dr. Kaplan?

9 DR. KAPLAN: Thank you. Now, with respect
10 to antimicrobial resistance, I wonder if we have an
11 idea of how much doxycycline is used overall each
12 year in the United States.

13 DR. MOORE: I'm sure those data are
14 available. I don't know who would have them.

15 DR. KAPLAN: I'm just trying to get -- I
16 don't know if Ed knows.

17 DR. COX: I think I can find it. Hang on
18 just a second. Just please go ahead. And if I
19 find it, I'll chime back in.

20 DR. MOORE: I'm very impressed with -- he's
21 got it sitting right here; He can get it. That's
22 pretty cool.

1 DR. KAPLAN: I'm just trying to figure out,
2 with respect to first responders, in a year or over
3 five years, what proportion would that mean for
4 overall use, 1 percent, 10 percent, 50 percent.

5 DR. MOORE: We'll come back to that when the
6 data are available.

7 Dr. Parker.

8 DR. PARKER: So I think, a part of that same
9 calculation, my question is, how much clarity do we
10 have about what a first responder is? I've been at
11 the table many times where there has never been
12 consensus about that. So I would like to know what
13 definition there is of what a first responder is
14 that we're thinking about, what the cohort size is
15 of that as we thinking about it, and how that would
16 be communicated.

17 There was also some discussion very quickly
18 that it's not clear if there would be verification
19 of whether or not you're a first responder. I'm
20 not sure how that would happen, either. But I
21 wonder if just so we could ballpark the cohort side
22 for the first responder, if we could know what that

1 means.

2 That's my first question.

3 DR. MOORE: And so your answer's coming
4 shortly. Go ahead.

5 DR. KORCH: Again, subject to the margins
6 around which local communities identify or can
7 self-identify what, for their particular needs,
8 first responders are, over the weekend I looked at
9 the Bureau of Labor Statistics just for what's
10 considered maybe a fundamental set of occupations
11 or groups, to include firefighters, police, and
12 sheriff's departments, so all law enforcement,
13 EMTs, as well as, in healthcare setting, nurses,
14 physicians' assistants, and physicians.

15 So if that is a core group of responders or
16 first responders -- and even that is fairly
17 inclusive -- the rough numbers come to
18 approximately I think about 7 or 8 million.

19 In addition to that, when one factors in
20 family members -- and again, this is back-of-the-
21 envelope rough calculations, so a rough order of
22 magnitude -- we're probably in the range of about

1 11 to 13, 15 million people with family members as
2 well as those other -- again, this is just raw
3 information from Bureau of Labor Statistics from
4 2010-2011, and it may not account for every single
5 other category.

6 Now, to the extent that we are looking at
7 the same issue in other contexts -- I think
8 somebody mentioned -- maybe Andy Pavia or someone
9 else; I can't recall who, maybe Jim James -- the
10 potential use of things like vaccines that we have.
11 We have a stockpile of vaccine that the first
12 responder community is also asked to have
13 availability as materials are being ready to
14 expire.

15 The federal government is looking at a
16 possible mechanism for using those as well. In
17 that particular context, what we are doing as far
18 as recommendation is for the state and local
19 communities themselves to define what is a first
20 responder. Again, that's a little bit more
21 nebulous than having specific categories of the
22 nature that I've just described. But I think, to

1 your point, or probable point, the notion of having
2 some flexibility, and yet at the same time having
3 some definitive capability of saying this group
4 does represent a first responder community so that
5 when individuals attempt to utilize this particular
6 way of providing themselves with a medkit, in
7 discussions with their physicians, there's a way to
8 verify that, some capability.

9 There are, of course -- there's a class of
10 individuals called certified first responders, so
11 there's a certification for first responders. That
12 would be an easy delineator right there. But
13 beyond that it becomes a little bit fuzzier.

14 DR. MOORE: So it sounds like -- if I
15 understand your statistics correctly, again, very
16 sketchy, but approximately 5 percent of the
17 population might be -- as much as 5 percent of the
18 population might be dispensed medkits.

19 DR. KORCH: Under the statistics, again,
20 back of the envelope.

21 DR. MOORE: Right. A lot of caveats in
22 those data.

1 Dr. Parker?

2 DR. PARKER: So one other specific question
3 was, the study that you mentioned the label
4 comprehension that I think you said was ongoing in
5 Maryland now -- I can't remember exactly.

6 DR. KORCH: Yes.

7 DR. PARKER: You mentioned that you had
8 other details about it. I'm just curious to know
9 if that label comprehension study is done using the
10 guidelines. The EUA that FDA authorized, that
11 became available in July of 2011, the initial one
12 did not use teaspoons and not mLs. And I'm
13 wondering if the study in the field is using what
14 we were provided here or what was available in July
15 2011 before this got modified.

16 DR. METZ: Sure. Matthew Metz from BARDA.

17 Just to make sure to clarify for everyone,
18 there are a couple of BARDA-sponsored studies that
19 Dr. Korch provided some information on. There is
20 an observational home preparation study that is
21 ongoing. And that one's actually being conducted
22 by Northland Labs outside of Chicago. And there is

1 a label comprehension study that is about to start,
2 and that'll be in the Baltimore region and parts of
3 Maryland.

4 There are milliliter and teaspoon
5 measurements provided in the instructions. And one
6 of the additions that we made to the kit to address
7 some of the concerns about accurate measurement is
8 a dosing syringe which, if you have one of the kits
9 in front of you, you can pull that out. That has
10 measurements on it in both as well.

11 So we tried to account for both ways of
12 reading the instructions so that the instructions
13 could be followed accurately, regardless of whether
14 it was in millimeters or teaspoons.

15 DR. PARKER: And then I had two questions
16 for the FDA. One was whether or not -- because
17 this would be a prescribed medication -- this
18 relates specifically to labels. One was, this
19 would be prescribed, and you'd get a prescription
20 for the prescription medication. And then it would
21 be kept in a home presumably, if it moved forward.

22 So I'm wondering if that means that there

1 would be federal oversight of the primary container
2 labels so that all of them would look the same,
3 rather than turning this to the state boards of
4 pharmacy for the primary label content, or would we
5 end up with this translated in 50 different states
6 on a primary container looking differently? Would
7 this be something that would come out of a federal
8 oversight, so it'd look the same across the
9 country. That's one question I have.

10 The other one relates to whether or not
11 there are any over-the-counter medications that
12 require compounding, and whether or not there's any
13 different oversight for something that would
14 require compounding like what's proposed here, and
15 whether or not there are different regulatory
16 oversight for that.

17 DR. LEONARD-SEGAL: Well, Ruth, you always
18 ask good questions. The OTC drug regulations would
19 not be applying to a prescription product, so I
20 can't really go to what that immediate container
21 would look like. If it were an OTC drug, it would
22 have to have all the characteristic requirements of

1 OTC drug labeling, as per the 21 CFR 201.66. It
2 would have to comply with all that, which would
3 include the drug-facts label, et cetera. It's a
4 different entity, so that's something that the
5 prescription folks are going to have to talk about.

6 In terms of OTC compounding, there are no
7 specific requirements for OTC drug compounding.
8 There are -- really, to the best of my
9 understanding, the people who look at compounding
10 really are compliance people. But within the CFR,
11 there are some regulations that detail specific
12 products that can be compounded by a pharmacist.

13 One thing I can tell you is that potassium
14 iodide, which is another counterterrorism entity,
15 has directions on it that allow or that require for
16 very young children, babies, infants, that the
17 product be mixed with either milk, or water, or
18 something like that.

19 So I think that there is a precedence for
20 mixing by a consumer for an OTC -- or for a product
21 that is in the home. It's not an OTC product, but
22 for a medication that's in the home. And I cannot

1 think of any OTC products that have been approved
2 with compounding instructions. The closest we get
3 is something like, "Take with food."

4 Does that help? Okay.

5 DR. PARKER: Yes.

6 DR. MOORE: For the transcriptionist, that
7 was Dr. Leonard-Segal.

8 Dr. Cox?

9 DR. COX: Yes. Hi. Just a couple other
10 comments, too.

11 Dr. Parker, your questions are good ones.
12 And I think one of the things, too, that makes it
13 challenging to answer right now is we don't
14 actually know what the configuration of the product
15 would be; is this going to be a box with something
16 inside of it; will a pharmacy label be put on the
17 top of it or something? So it's really just
18 beyond -- I think we probably need to have a better
19 understanding of what the product will look like to
20 be able to answer your question, which is a good
21 one.

22 I take from your question that one of the

1 things that I think you're getting at is
2 consistency and that the material on the bottle be
3 informative and such. And it seems like that's
4 part of what you're getting at.

5 DR. PARKER: And who's going to watch it?

6 DR. COX: Can you help me understand that
7 just a little more?

8 DR. PARKER: Yes. That would be sort of
9 regulatory oversight, that it looks the same
10 across, and who would be doing that; and whether or
11 not that would be a part of the charge up front.
12 And if this were deemed to be an issue needed for
13 public health, that it's actually not just
14 something that is recommended, but something that
15 actually ends up occurring.

16 DR. COX: Right. So that's getting to the
17 key point of the testing and evaluation of the
18 actual packaging and materials, and are they able
19 to be used as expected and anticipated, and are
20 there certain things that need to be on there in
21 order for folks to be able to use them
22 appropriately

1 So, yes, a good point. Then the other
2 thing, too, is with regard to some of the crushing
3 and mixing that I think it underscores. And
4 certainly from the work that's been done so far,
5 there's been some important lessons learned about
6 in which food substances the drug is stable or not
7 stable, can uniformity of the drug be achieved with
8 regard to distribution within the food substance,
9 and all those sorts of questions.

10 Again, another good question, and for those
11 same reasons why the testing is being done; to be
12 able to understand whether the food mixtures will
13 be able to be utilized, and if so, which foods, and
14 which will mask the taste and deliver drug
15 appropriately.

16 Back to Dr. Kaplan's question?

17 DR. KAPLAN: Yes?

18 DR. COX: So we did I think in either late
19 2010 or 2011 published -- so this is on our FDA
20 public website -- put forth figures with regard to
21 the sales of antibacterial drugs for human use
22 during the calendar year of 2009.

1 Let me just get these numbers here again.
2 Actually, I've got them here.

3 So this is wholesale data, so this is the
4 amount of drug that entered into either the retail
5 or the non-retail chain for the year 2009. And the
6 numbers are in kilograms, so it's number of
7 kilograms sold in the United States. And, again,
8 information about drug supply is sensitive
9 information. But this is on our FDA public
10 website, so it's already out there. So I'm not
11 telling you anything you couldn't find from just a
12 little more searching.

13 The amount of doxycycline was
14 59,535 kilograms. And another figure I'll just put
15 out there, too, that's also in that same public
16 document, the tetracycline class agents, the total
17 for the year 2009 was 131,137 kilograms, so
18 131,137 kilograms for the year 2009. And I
19 realize, too, that still leaves some more math to
20 do because we've got to get from kilograms to other
21 weight measures and such.

22 DR. MOORE: I'm sorry. Dr. Cox, could you

1 provide the website for that?

2 DR. COX: Yes. I can. Hang on just a
3 second here. So the website, what's the best way?
4 It's a long tag here. I mean, I can read it so
5 it's in the record.

6 DR. MOORE: Sure.

7 DR. COX: Okay. So it's
8 www.fda.gov/downloads/drugs/drugsafety/information
9 [bydrugclass/](http://www.fda.gov/downloads/drugs/drugsafety/information) --

10 DR. MOORE: All one word?

11 DR. COX: -- ucm261174.pdf. And as
12 Dr. Moore stated, that's all one word, so there's
13 no spaces in between any of that.

14 DR. MOORE: I'm sorry. So
15 "informationbydrugclass," that's all one word, then
16 forward slash. And then you said -- could you give
17 me the UCM and the numbers again?

18 DR. COX: Yes. So it's UCM261174.pdf.

19 DR. MOORE: Excellent. Thank you very much.

20 DR. COX: Okay.

21 DR. MOORE: Exhausted.

22 Dr. Curry, you had a question about whether

1 this was veterinary use.

2 DR. CURRY: I'm sorry. Did that include
3 veterinary use as well?

4 DR. COX: That did not. That's human use.

5 DR. CURRY: Okay. Thank you.

6 DR. MOORE: Dr. Gellad, you had a question.

7 DR. GELLAD: Yes. I'm going to do three
8 quick questions in case any other websites come up.

9 [Laughter.]

10 DR. GELLAD: I just want to get my questions
11 out. The first is about -- I'm trying to think in
12 terms of the answer to the first question, what are
13 the benefits of the medkit over and above a bottle
14 of doxycycline? That part of the IOM
15 recommendation stuck for me. And I'm wondering
16 what are the advantages of a medkit over
17 doxycycline?

18 It seems like the two issues are, one, we
19 assume that people will be less likely to take them
20 unless they have a special kit that says, "Open
21 only in emergency." But that may be something that
22 can be tested, whether that really is true. The

1 other, it seems like everything else in the medkit
2 is dedicated just to making sure those who can't
3 take pills can take the medication.

4 So those are my thoughts. Are those the two
5 reasons why we need a medkit as opposed to a
6 bottle, and are those worth the costs and all of
7 this discussion?

8 The second point is if anyone has considered
9 the medical legal reasons. This is kind of like a
10 prescription versus OTC product. If I give my
11 patient a prescription, and they use it a year and
12 a half later, and they have an adverse effect, are
13 there any legal issues in terms of my own backside?
14 I guess, to put it bluntly.

15 The third issue is this -- for some reason,
16 when I think about these, I think about narcotics.
17 And it brought up the issue before about who's
18 going to get these. And is it going to be verified
19 at the point of the pharmacy, or at the
20 prescription, if someone is a first responder? If
21 they lose their medkit and need another one in a
22 week, can they get one? Can they get two? Can

1 they get three? What are the issues about how
2 these will be distributed to those who probably
3 aren't indicated in the same way that other
4 products also are?

5 Anyone can answer or not answer, I guess,
6 but I'd be curious about the first question, which
7 is, what is the benefit of the medkit over simple
8 doxycycline?

9 DR. YESKEY: Hi. Deb Yeskey from BARDA. I
10 can definitely take that first one. It is a
11 deterrent, actually, for opening -- the packaging
12 is special to deter people to open it. The
13 differences between a bottle of doxy just sitting
14 on your medicine shelf rather than something that's
15 kitted, again, this would be the household members,
16 too, so there would be multiple bottles of doxy in
17 there. So you want to keep them all together. One
18 would want to keep them all together so they're in
19 a safe storage space, again, temperature
20 controlled, away from pets, away from children.
21 It's a nice, convenient way to do that.

22 But I think one of the biggest things is the

1 deterrent for opening a bottle. You're less
2 likely -- or one would think you are less likely to
3 open something that is just a prescription bottle
4 rather than something that has specific labeling on
5 it to make sure that you open it at the time of an
6 event and not before.

7 DR. GELLAD: Has that been actually tested,
8 or is that our assumption? If we're targeting this
9 toward first responders or people who might have
10 some knowledge about when it should be used.

11 DR. YESKEY: I think that -- we haven't done
12 a test head to head against a prescription bottle
13 versus the kit. And again, we're here to get your
14 comments and recommendations. So as Matt has
15 mentioned, we're not done with looking at things
16 like this. So your comments and suggestions are
17 welcomed, and doing something head to head like
18 that would probably be beneficial.

19 DR. MOORE: Thank you. Was there a comment
20 from the FDA before we move on?

21 DR. COX: So maybe I'll try to make some
22 brief comments. As Deb said, ways to essentially

1 evaluate and understand what these instructions and
2 the packaging will do -- one of the reasons we're
3 here talking about this here today is that it's not
4 part of the current approved product labeling. So
5 these are additional materials. And evaluating
6 them would help us to understand how they perform.
7 And that's one of the pieces of scientific
8 information that would then help to understand what
9 information would be included in such a product.

10 So because they are not part of the current
11 product and they need to be evaluated in order to
12 understand how they perform, it's part of the step
13 along the way in essence of an evaluation of such a
14 product.

15 The legal issue question, I don't think we
16 can answer that too much. I mean, that sounds like
17 it's getting to issues around medical liability, so
18 probably beyond what we can answer.

19 Then your other question was who could get
20 this and such. Obviously, there's issues of what's
21 in the product label. There may be programmatic
22 issues around how a product might be made

1 available. And then there's also practice of
2 medicine issues. And I think your question sort of
3 brings all three of these together, so depending
4 upon which perspective you're looking at, you may
5 come to a slightly different answer.

6 Under the practice of medicine, physicians
7 can write prescriptions for products that are out
8 there and available. There can be various
9 different ways of mitigating risk and such, and
10 various steps along the way that might also be part
11 of that. But that's the broad scope I think of
12 your question and what you're bringing up.

13 DR. MOORE: I have a question for
14 Dr. Lynfield if she's here.

15 Dr. Lynfield, my question really is, it came
16 up in the Medline search that antibiotic use in
17 Europe could not be -- that is, over-the-counter
18 antibiotic -- the ability to acquire antibiotics
19 over the counter in Europe could not be generalized
20 to make predictions in the United States, the idea
21 being that northern and western Europeans use
22 antibiotics over the counter rather relatively

1 sparingly compared with those in southern and
2 eastern Europe.

3 So my question to you is -- I'm sorry I'm
4 taking forever to get to the point. The question I
5 have is do we have any data on the ethnic makeup of
6 the people in your study? Because I know Minnesota
7 is a homogeneous place -- I'm sorry, a
8 heterogeneous place, but it does have a tradition
9 of homogeneity. And my question is I don't know
10 how many northern Europeans consisted of
11 individuals in your study.

12 DR. LYNFIELD: We didn't ask them if they
13 were of northern European origin, but we did ask
14 their race, and 90 percent were white. And close
15 to three-quarters of them did have some college
16 education.

17 DR. MOORE: Thank you. My point is in terms
18 of generalizing for the rest of the country.

19 DR. LYNFIELD: Yes. Absolutely. That was a
20 point I made, that I think it is difficult to
21 generalize that population to other populations.
22 And I think it would be important to evaluate other

1 populations.

2 DR. MOORE: Thank you very much.

3 Ms. Young, you had a question.

4 MS. YOUNG: I just wanted to clarify. Would
5 this be a precedent in terms of individual
6 stockpiling versus government stockpiling? Is that
7 what we would be promoting if we go forward with
8 this, if someone from defense could address that?

9 Also, I just wondered where this fell in
10 terms of alternative ways to deal with an anthrax
11 attack, such as the vaccine or the mask that was
12 mentioned. If we go forward with this, will we be
13 taking our eyes off the price in finding something
14 maybe less cumbersome?

15 So those are my two major questions. Thank
16 you.

17 DR. MOORE: Let me do this. I wanted to
18 have this particular session before we get too much
19 further to clarify any issues that were brought up,
20 but I promise we're going to get to the general
21 discussion here in a second.

22 Let me ask one question of the FDA.

1 Does the FDA have any data -- it was
2 mentioned earlier that the REMS for narcotics is
3 being evaluated as a potential source of data or an
4 experience upon which medkit distribution could be
5 based. Do we have any data on the REMS for
6 narcotic distribution?

7 DR. COX: I don't think we have any -- at
8 least, I don't; others may have more information
9 about the REMS for narcotics distribution. When
10 you think about REMS, you think about medication
11 guides, communication plans, and elements to assure
12 safe use. And when you start to get to restricted
13 distribution, you're generally talking about issues
14 around elements to assure safe use.

15 If we think about product that start to fall
16 under that category, it may be drugs that are
17 teratogenic, have particular safety issues, that
18 monitoring is needed before the product would
19 become available.

20 So I just throw that out there as just some
21 general information about REMS programs in general,
22 recognizing the scale, and as one moves up the

1 scale to restrict the distribution, typically, the
2 types of products that fall under those categories.

3 For the opioid question, I don't
4 believe -- I don't have any data myself to be able
5 to share on it.

6 Was there something in particular you were
7 wondering about?

8 DR. MOORE: No. I was just wondering if we
9 could learn from the experience, if there were any
10 data that we could get access to, to learn from
11 that experience because that, to me, I would
12 imagine to be a more significant potential for
13 unauthorized package opening than antibiotics in
14 emergency.

15 DR. COX: Yes. I can't think of anything in
16 particular, and I don't know that data well enough
17 to be able to contribute something specifically
18 that would answer your question, Dr. Moore. Sorry.

19 DR. MOORE: No. No problem at all. Thank
20 you.

21 So that takes us to the end of the
22 clarification questions. Let's move, then, to the

1 general discussion questions. And, Dr. Fischhoff,
2 I do believe you had a question.

3 DR. FISCHHOFF: Thank you.

4 So the public health questions have an
5 efficacy interpretation. We have an obligation to
6 do things as well as we possibly can and to
7 characterize the quality of our evidence so that
8 people who need to make these decisions can do them
9 in as well-informed a way as possible.

10 But these are also questions of public
11 policy, and we're dealing with a program that's a
12 matter of national security. And there's been a
13 theme that's kind of woven in and out of the
14 discussions. So I'd like just to make certain that
15 we at some point discuss what are the fundamental
16 political assumptions that are being made in the
17 program that we're talking about.

18 So there's a discussion. So we have a
19 question of what's our obligation to the first
20 responders? There's a question of what's our
21 obligation to people who do and don't have money?
22 What's our obligation to people who have ready, who

1 can follow instructions easily, and can't because
2 of disability or the language that they speak?

3 I feel like we have an obligation to -- I
4 don't know that we're -- we're technical experts,
5 so we're tasked with helping to do this as well as
6 possible. I think that perhaps the way we can
7 inform our national decision makers is to flag
8 these issues and say, "Here will be the winners and
9 the losers. Here's how you are going to be judged
10 in the light of history if we need this program, if
11 it goes astray," and not so that they can make that
12 kind of decision.

13 I was on the Department of Homeland
14 Security's science and technology advisory
15 committee from the beginning until it stopped
16 meeting. And we had one discussion about, what was
17 our national strategy? What was the X document for
18 this current struggle that we're in? And our
19 chair, General Welch, made the point that our
20 overall strategy ought to be to try to ensure the
21 continuity of the American way of life so that
22 people have faith in their society that it works

1 for everybody.

2 So somehow or other, I don't want that to
3 get lost in our worry about executing -- I don't
4 want us to be executing the wrong strategy or one
5 that will undermine our national security in the
6 most efficacious way possible.

7 DR. MOORE: Thank you. Let me get
8 back -- sorry. Ms. Young -- nobody stepped up to
9 answer Ms. Young's question from before. I wasn't
10 sure if anybody could do that now.

11 Ms. Young, would you mind rephrasing your
12 question?

13 MS. YOUNG: I had two questions. One was,
14 is this a precedent-setting move if we have
15 individuals homes stockpiling versus government
16 stockpiling? And the second question was, where
17 does this fall in terms of alternatives to deal
18 with the counterterrorism for anthrax?

19 So are we going to be using a lot of
20 resources, money, to go forward with studies and
21 such that maybe could be applied in terms of
22 alternatives that may be as efficacious or more

1 efficacious? Just some general comment on that
2 would be helpful.

3 DR. MOORE: Dr. Cox?

4 DR. COX: Probably -- no, Dr. Korch, please.
5 I didn't quite know who all was going to respond to
6 it. I want to comment, too, on Dr. Fischhoff's
7 comment, and that'll give Dr. Korch just a minute
8 as he makes his way up to the microphone.

9 I think he's focused in on a very important
10 issue here. And I think, as we've tried to prepare
11 for this meeting, one of the things we've realized
12 is that sometimes it's difficult to separate out
13 what are sometimes probably more programmatic
14 issues from the technical development issues of a
15 study that you might do to characterize a
16 particular aspect of a package, or a program, or
17 how a product might be produced.

18 I think that's a key point, and I want to
19 thank you for the comment because I think it really
20 helps as one tries to think about the issues that
21 we're facing here today.

22 Then Dr. Korch, I'll defer to you on the

1 questions about other areas where there have been
2 stockpiles, and then some of the tradeoffs and
3 programmatic issues.

4 DR. KORCH: I'm going to start with the
5 tradeoff, the programmatic issues first. Then I'll
6 ask you to repeat the first part because I've been
7 thinking through all of the various aspects of
8 questions and answers here.

9 With regard to the relative importance of
10 this particular initiative or effort to all the
11 demands, there are tremendous numbers of demands.
12 And as part of this overall PHEMCE that I
13 described, this interagency process, on a biweekly
14 basis and on a regular basis, we're looking at the
15 costs and tradeoffs of the multiple programs within
16 anthrax as a function of this generation of vaccine
17 versus next generation of vaccine, next generation
18 of vaccine versus an adjuvant next generation of
19 vaccine. What advantages do you have? What
20 tradeoffs? What are you losing? What are you
21 basically sacrificing for making a particular
22 investment in a way?

1 Similarly, anthrax versus smallpox versus
2 botulinum versus tularemia or Burkholderia, where
3 do you put that relative priority? And then
4 again, in terms of the relative return on
5 investment for any one of these individual's
6 efforts, it unfortunately doesn't necessarily break
7 down to a nice, easy algorithm, plug on in, and get
8 an answer on out. So there's a relative or
9 qualitative value to investments.

10 I can probably say that relative to many of
11 the other large issues that we're facing with
12 pandemic flu, with some of the stockpile issues,
13 the big purchases that have to be made, maintenance
14 of the stockpile, operational concepts, et cetera,
15 this is not one that is pulling off huge amounts of
16 resources.

17 We have the bandwidth to tackle a number of
18 issues simultaneously, both within ASPR, at CDC,
19 NIH, as well as our colleagues at FDA that do
20 participate with us in making these decisions, or
21 assisting in making the decisions at the level of
22 the senior leaders that ultimately bear the

1 responsibility for how these investments are made,
2 as well as notifying Congress and the GAO, and
3 everybody else in terms of defending why you made
4 that decision and how it had relevant impact and
5 relative value to everything else that you have to
6 do.

7 Now, can I ask you to restate the first
8 question?

9 MS. YOUNG: The government has stockpiled
10 drugs to deal with these terrorist attacks in the
11 past. Is this a precedent that you'd have
12 individual homes stockpiling drugs to deal with the
13 potential terrorism attack?

14 DR. KORCH: Okay, so a precedent. This is
15 certainly an aspect that we think adds value to the
16 entire capabilities that we want to bring to bear.
17 So precedent -- I don't quite know how to address a
18 precedent.

19 MS. YOUNG: Is this the first time?

20 DR. KORCH: This is the first time. This is
21 the first time. Yes. I'm sorry. Yes, okay. I
22 got that.

1 To the best of my knowledge, aside from KI,
2 home stockpiling KI, this is the first time that
3 we're addressing or have continued to press to
4 address this particular need. Yes.

5 DR. MOORE: Dr. Landis?

6 MS. LANDIS: First, I just want to go back
7 and just clarify. Dr. Parker had asked a question
8 about this medkit, and this is from a pharmacist's
9 perspective.

10 If this is a prescription that's going out,
11 it would be labeled on the outside of the package.
12 It would be really easy to put the expiration date
13 so that the bottle inside would have that
14 information that was on there originally. So this
15 would be a unit of use that could go out, depending
16 on what that final product was.

17 Could you put multiple families in this?
18 That probably wouldn't fit as a prescription item,
19 a separate bag, so each person is liable,
20 especially if you have kids. And, again, this is
21 under friendly times. We're not under attack or
22 anything. It would just be going out as a

1 prescription to the first responders. So just some
2 clarification on that.

3 The second thing is, I'm having a difficult
4 time trying to think about what does a first
5 responder get versus what goes out to the general
6 population. And I think we really need to look at
7 it closely, that whatever that is, I think there
8 should be some consistency because we don't want to
9 have that idea of the haves and the have-nots.

10 It should be simplistic across the board,
11 regardless of what their education level is. Bring
12 it down to the level that 80 percent of the
13 population can understand or 90 percent of the
14 population can understand. Don't have one that's
15 set for first responders, then let's come up with a
16 package for something else. Make it simple so that
17 it can go out and be dispensed.

18 Another question I have with that is, what
19 happens with the follow-on? What happens with that
20 other 50 days? Say I have this medkit in my house
21 for four years, and I'm now utilized to use that
22 10 days. How do I go about getting that other

1 50 days? I may not have had that same physician
2 for years. As you know, different insurances,
3 different physicians, different practices.

4 So what kind of things can be put in place?
5 And I think those are the kind of questions that
6 really need to be addressed here, is how do we
7 ensure that a person, if they start this, is going
8 to be able to complete this? Is that through the
9 utilization of pharmacists as being that gatekeeper
10 there to make sure that people are following
11 through with the medication, not just at 10 days,
12 but the other 50 days?

13 So I think those are the kind of questions
14 we really need to look at here as we move forward.

15 DR. MOORE: Thank you.

16 Did you have a comment?

17 DR. GORMAN: Yes. If I could address how do
18 you get the follow-on 50 days. Sue Gorman, CDC.

19 We envision that people that don't have a
20 first responder medkit in their home are going to
21 go to what George referred to earlier as points of
22 dispensing. And the cities have all planned to set

1 up these points of dispensing so the general
2 population can receive their prophylaxis. That's
3 where they'll receive their first 10 days.

4 Again, if they have a first responder medkit
5 in their home for the follow-on 50 days and for the
6 general population, they would again go to the
7 points of dispensing to get their follow-on
8 50 days. So they would see another person after
9 their first 10-day supply. It would be determined
10 whether or not they would need to continue on with
11 the next 50 days' worth. But that would occur at
12 the points of dispensing in the community.

13 DR. MOORE: Thank you.

14 Ms. Landis, did you have something you
15 wanted to say further?

16 MS. LANDIS: Again, how do you know if a
17 person that's coming in has actually taken that
18 10 days? So again, I don't know how you're looking
19 at it with the registry that you have. I just
20 think there's a lot of questions that need to be
21 answered in that area or looked at.

22 DR. MOORE: Thank you.

1 Dr. Morrato?

2 DR. MORRATO: Yes. I actually wanted to
3 respond to also Dr. Parker and Dr. Landis' comments
4 in terms of precedent for a kit before.

5 I had worked on the development of Helidac,
6 which was a kit for triple therapy for h. pylori
7 that had bismuth, which was OTC Pepto,
8 metronidazole, and tetracycline. And so the value
9 of packaging it was so that you could have a common
10 label and that you could also put in a lot of
11 information on education. So it allows uniformity.
12 Now, one of the issues with it is that it had drugs
13 that were already commonly available, and so the
14 value is in the packaging, but it was easily
15 substituted with pharmacy.

16 So I think that's something that needs to be
17 looked at, that even if we've done this wonderful
18 job with a great kit and all this information, how
19 will pharmacies respond and will there just be
20 natural substitution with what's already available.
21 So that was one question.

22 Then the other one, building on Dr. Day's

1 comment, I agree with her 100 percent in terms of
2 the naming of the kit is very important. And I
3 would go one step further in that it's really not a
4 medkit; it's a starter kit. I mean, I think people
5 need to think of this as it's just starting them
6 out; it's not the treatment. And that seemed to be
7 one of the issues that came up in one of the
8 studies.

9 Then I also did a quick search on how much
10 doxycycline. IMS Health has the top 200 drugs that
11 are prescribed, which is another data source. And
12 they list the top 200 drugs for 2010. And
13 doxycycline is 150. They don't say how many
14 prescriptions for that, but number 20 on their list
15 is 21 million prescriptions.

16 So I think you were saying 10 to 20 million
17 people might fall within the responder community.
18 And that's equivalent probably to the high end of
19 that top 200 list. So I would expect that what
20 we're looking at is a sizeable increase in terms of
21 the population that would be taking doxycycline.
22 And we can get the exact numbers, et cetera, but it

1 gives us some framing I think.

2 DR. MOORE: Thank you.

3 Dr. Wolfe, you had a question?

4 DR. WOLFE: A general comment. It seems to
5 be agreed by the entity that proposed at the IOM,
6 and now in the framing of the FDA question, and by
7 the sponsor, that we for now have given up on the
8 idea of general community predisposing and have
9 focused more on the first responders. And once we
10 make that move, part of the reason for the medkit,
11 which is that the non-first responder part of the
12 population may be more likely to misuse something
13 other than a medkit, we have taken that away.

14 So I want to read now -- this is on page 204
15 of this extraordinary IOM document. I did look at
16 the whole thing. And this goes to the point that
17 was just raised by Dr. Gellad about what's the
18 evidence for the regular prescription versus the
19 medkit? This is what they said.

20 "Do not pursue development of an
21 FDA-approved medkit unless this is supported by
22 additional safety and cost research." And this is

1 what they say. They do allow for the possibility
2 for the first responders.

3 "The committee does not recommend
4 development of an FDA-approved medkit designed for
5 prepositioning for an anthrax attack until and
6 unless research demonstrates that the medkits are
7 significantly less likely to be used
8 inappropriately than a standard prescription and
9 can be produced at costs comparable to those of
10 standard prescription antibiotics."

11 You just heard in the answer given by the
12 sponsor to Dr. Gellad's question that they have not
13 done such a head-to-head test.

14 I would say that the differential between
15 the medkit and the standard prescription lessens,
16 at least theoretically, when you take away the
17 general population from the equation. So I think
18 that this is part of discussing question number 1.

19 This IOM report comes out in November with
20 these kinds of very strong statements and an
21 extraordinary amount of research and
22 thoughtfulness. I mean, a lot of the discussion

1 that we've had here today I think would have been
2 informed by seeing more. We had little pieces of
3 it in the sponsor's briefing package, but the whole
4 report is really extraordinary.

5 So I think that we need to step back a
6 little bit instead of just assuming, medkit is
7 given -- remember, it's the month after this IOM
8 report that the IND is filed by the sponsor for the
9 medkit. They've already more or less decided the
10 issue between the medkit and the regular
11 prescription. The cost is going to be enormously
12 different.

13 FDA does have the authority, which it has
14 not used often enough, to put in medication guides.
15 So you can imagine the combination of an
16 FDA-approved medication guide plus even a regular
17 prescription may at least go a way toward giving
18 some of the information that is now just in the
19 medkits.

20 So just a general comment, and this
21 particular statement by recommendation 5.5 on page
22 204 should be a basis for at least some of our

1 discussion in question 1 and question 2.

2 DR. MOORE: Thank you, Dr. Wolfe.

3 Dr. Reidenberg?

4 DR. REIDENBERG: Yes. A number of comments.
5 Firstly, we're talking about how the prescription
6 will limit the distribution. I was practicing in
7 New York City when we had our anthrax scare. And a
8 number of personal friends kept calling me for
9 prescriptions for cipro. So I think that once it's
10 publicized -- and it will be publicized -- that
11 first responders and their families have these
12 medkits, I don't know that I can predict that some
13 people who are not first responders will go to
14 whoever is prescribing for them to get a personal
15 prescription for the equivalent medkit that they
16 should be prepared also.

17 Then I begin to worry how many people who
18 are scared, but not exposed, will take the
19 tetracycline or cipro that they have with no
20 possibility of benefit and the possibility of
21 acquiring thrush, monilia? I'm concerned about
22 C. diff. in people who just take antibiotics. And

1 will we be making more mischief than we're possibly
2 preventing?

3 Secondly or next, the medkit scenario
4 specifically says physician would prescribe for
5 family members at their request. As an internist,
6 I have no professional relationship to the children
7 of my patients. Many women of reproductive age in
8 New York only see a gynecologist. And so it would
9 be interesting if there's been any surveys of the
10 realities of medical practice to see how many
11 different prescribers a family would have to see in
12 order to get prescriptions for each member, or if
13 it's being suggested that I should violate my New
14 York State medical practice rules in order to
15 prescribe for everybody.

16 Then we've already talked about the question
17 of people are paying 50, \$60 for a family's worth
18 of medicine. Are they really going to throw it
19 away and do that every couple years, or are they
20 going to keep it for a longer period?

21 I can't help but be reminded of the
22 decades-old fallout shelter craze, where

1 individuals were urged to make themselves fallout
2 shelters and stock them with canned goods that
3 would be stable in case. And so this sure has many
4 of the appearances of that, where it's assuming
5 that everybody in the United States will know that
6 we have doxycycline available for everybody, but no
7 organizations that might want to launch such an
8 attack would be aware of it. And so they would
9 attack with doxycycline-sensitive anthrax.

10 DR. MOORE: Those are good points. Thank
11 you.

12 I'll throw in a little anecdote. I was
13 practicing in Wichita when 9/11 occurred and the
14 anthrax attacks. Now, there were no anthrax
15 attacks 50 miles west of the east coast. But the
16 urologist kept stockpiles of cipro on hand for free
17 samples for their Medicare patients on whom they do
18 biopsies and whom can't afford standard cipro
19 prescriptions. All of their samples disappear
20 mysteriously from their closets.

21 I had legions of physicians -- physicians,
22 who ought to know better -- calling, wanting

1 prescriptions for cipro, not for doxy, but for
2 cipro. And then, of course, many of them took the
3 cipro.

4 So my lesson there was that physicians can't
5 be trusted.

6 [Laughter.]

7 DR. MOORE: Dr. Totman, you had a question.

8 DR. TOTMAN: I wanted to ask FDA today
9 whether there's any currently available RX drug
10 that has the MedWatch forms packaged with it.

11 DR. COX: So this is just from memory. I
12 can't think of an approved prescription product
13 that has a MedWatch form attached with it. I mean,
14 it is available on our website and such now. There
15 have been other EUA products that have been out
16 there that do have either a MedWatch form, or a
17 reference, or a link to a MedWatch form that I can
18 recall. But obviously, the number of products
19 under EUA is small.

20 DR. ALEXANDER: Almost all of the new
21 products that have PLR, the new physician labeling
22 rule format, will include contact information with

1 regard to the MedWatch and the med guides, but not
2 the forms themselves.

3 That is part of the issue that we're sort of
4 dealing with. A lot of the format of the kit is
5 essentially a remainder from its initial
6 development as a product that was intended for the
7 emergency use authorization purposes and testing.
8 And so the issue in part is that there are some
9 aspects of the kit. And what we've proposed, that
10 may be important for testing, just on the basis of
11 the fact that if the SNS stockpile basically has
12 huge numbers of 100-milligram tablets that's going
13 to be used in an event of mass exposure, and that
14 that treatment will need to go to children, then
15 potentially the testing of the instructions for how
16 to crush and dose would probably be needed,
17 regardless of whether it ends up packaged as part
18 of a medkit or not.

19 But that is an important aspect to keep in
20 mind, that much of this may in fact be a remnant of
21 the fact that it started as a kit through the
22 emergency use authorization.

1 DR. TOTMAN: I guess a related question for
2 the sponsor is, I noticed in the written materials
3 that it was said that the instructions and warnings
4 would be both on the outside pouch as well as on
5 the inside. I notice what we saw didn't have
6 anything on the inside.

7 DR. MOORE: Let me interject for a second.
8 For the transcriptionist, that was Dr. Alexander
9 speaking before, and then Dr. Hilton asked a
10 question. And then now, we'll go to the sponsor.

11 Dr. Totman. Sorry. Then we'll go to the
12 sponsor.

13 DR. YESKEY: Deb Yeskey, BARDA. Yes. So in
14 your written materials, we described our kit for
15 the USPS, and that's truly how it is. It's the
16 same sort of bag. It's a tamper-evident bag, where
17 we have the exact same written materials inside the
18 pouch and then on the outside. These kits that you
19 saw were for our label comprehension study, so
20 they're a little bit different. They're modified,
21 just like Matt said, a little bit from our USPS
22 actual kit.

1 DR. TOTMAN: And the expiration date would
2 only be on the immediate container?

3 DR. YESKEY: Well, depending,
4 again -- prescription label, that's why the back
5 part of the bag is transparent, so it's easily
6 readable to see the bottles, the expiry date of the
7 bottles, but it could be also on the prescription
8 label as well.

9 DR. TOTMAN: It would take a very motivated
10 person to look for the expiration date, so for
11 something that might be important, that maybe
12 should be on the outside as well.

13 DR. YESKEY: That could definitely be a
14 possibility once it's dispensed. The pharmacist
15 could write that expiry date on the bag.

16 DR. MOORE: Thank you.

17 Dr. Hilton. Now, we're with you.

18 DR. HILTON: Thank you. I feel that we
19 haven't been presented enough with epidemiology of
20 exposure, the relationship between exposure to
21 anthrax and incidence of morbidity and mortality.

22 If someone is, for example, indoors with

1 windows closed, are they exposed when there's also
2 widespread airborne dissemination of anthrax, and
3 do they need treatment or do they not? Is somebody
4 outside playing soccer at that time in need of a
5 different dose than somebody who is indoors
6 reading? Does everybody need 60 days of treatment?

7 I just feel that too many unanswered
8 questions exist right now about the relationship
9 between exposure and disease and the need for
10 treatment.

11 DR. MOORE: Thank you. I suspect that that
12 particular issue, while a very important one, lies
13 outside the scope of discussion for this committee,
14 unless, Dr. Korch, you'd like to handle that.

15 No? You're going to take a pass. Okay.
16 That's fine.

17 As I say, it's an important question, but,
18 really, I think it's again sort of unanswerable at
19 this point, I would imagine.

20 If that's all right, let's move into --

21 Sorry. Dr. Cox, you want to take a stab at
22 that?

1 DR. COX: No.

2 [Laughter.]

3 DR. COX: Just a comment, though.

4 Where Dr. Fischhoff brought up the issues
5 around technical issues in the design of a study
6 and programmatic issues, I've heard some of the
7 discussion -- and I think folks are also knocking
8 on the door of another issue -- and maybe it's out
9 there, and it was definitely in the IOM
10 comments -- and that is the issue of availability
11 of a medkit product. And then we also know that
12 doxycycline is a prescription drug that has been
13 available for years.

14 So it's just one other thing that I think
15 adds to the complexity of the situation that we're
16 dealing with. And it's been talked about, and I
17 just wanted to just mention that again because I
18 think it's come up again in some of the comments
19 that we're hearing.

20 DR. MOORE: Thanks.

21 Dr. Walker?

22 DR. WALKER-HARDING: I was just looking more

1 at the public health implications, the bigger
2 picture, looking at the overall need for our
3 country to have more disaster preparedness, and
4 seeing this as the beginning of a system to get us
5 moving along that direction. I see this as
6 possibly a fundamental and good thing for us to
7 begin to continue walking down the path, because if
8 we can figure out how to help the first responders
9 and their families first, going that next step of
10 working with the rest of the population is going to
11 be that much easier. I think biting off trying to
12 do this for the whole population initially is
13 probably going to be fraught with a lot of
14 problems.

15 The other thing, we talk a lot about misuse,
16 and people understanding labeling, and they
17 shouldn't need to see a doctor. I'm not really
18 sure that a doctor or a pharmacist always has that
19 much impact on how well people take their
20 medication anyway. There's a lot of misuse of
21 medication, period. People make their own
22 decisions about how they're using the pills that

1 they get.

2 So I don't think -- unless we had a head-to-
3 head study -- and I think we wouldn't like the
4 results of it. Looking at how well a doctor tells
5 a patient to use their medication, how well a
6 person listens to a pharmacist, I think we would be
7 very surprised. To me, when you see people doing
8 well with their medicine, it's because the
9 instructions that they have when they go home are
10 understandable. What they hear somebody say
11 earlier may or may not be of any use.

12 So I think those are logistical things. How
13 do we dispense it? How do we figure out for people
14 who may be challenged in understanding how to take
15 medicine? How do we figure the majority of people
16 can understand that? How do we label it? And
17 those are kind of logistical things in an overall
18 strategy for trying to find a way to address a
19 chemical bioterrorism event. And if we can figure
20 out with this, then let's say we need another drug
21 or we need some other medication; we can still use
22 that same system to get it out to people.

1 So I think it's important to look at the
2 logistical things. But overall, to me, to not do
3 this would leave something open that we should be
4 addressing.

5 DR. MOORE: So we're coming up on the 3:00
6 break. I'm going to entertain just a few more
7 questions, then I'm going to have to impose a hard
8 stop, after which we'll discuss each of the
9 questions.

10 So Dr. Rogers?

11 DR. ROGERS: I'm going to go back to the
12 cost. If first responders are using it and it's
13 set at a certain price, what guarantee would we
14 have -- or would there be any type of way to the
15 general public that it would be still at that rate?
16 Because what we've known is that prices go up as
17 there is demand. And that really would concern me
18 because that means that we're depriving certain
19 people from getting this.

20 DR. MOORE: Thank you.

21 DR. LEONARD-SEGAL: I can try to take a stab
22 at that. FDA does not control pricing of

1 medication. And so I think that it's difficult to
2 make decisions around these kinds of issues with
3 prices in mind. It's also very difficult from our
4 experience on the OTC side, when we have had
5 companies that have been looking at a particular
6 product, and in our actual-use studies, people will
7 generally purchase the product as part of the study
8 design, and they get reimbursed for it at the end,
9 although they're not told up front that they're
10 going to be reimbursed for it at the end.

11 We've had companies that have been very
12 interested in our entertaining the importance of a
13 purchase decision. We never look at that with
14 great interest. We look at self-selection based
15 upon the ability to determine what's on the label
16 and whether the individual who's reading the label
17 can actually self-identify that they have the
18 condition for which the drug is indicated, and that
19 they have the other medical history requirements to
20 use or not to use the drug, whether they can make a
21 proper decision.

22 That's what we're interested in, because we

1 know that prices can change, and they do. And we
2 don't have any control over that.

3 DR. ROGERS: It was more of a rhetorical
4 type question.

5 DR. MOORE: Thank you both for your
6 questions and your answers.

7 Dr. Curry?

8 DR. CURRY: As I sit here, I'm trying to
9 step back and think what the big picture is and
10 what exactly we're trying to accomplish with this.
11 For example, would providing this to first
12 providers, much less to the general public,
13 actually prevent us from having to mobilize a
14 national stockpile and set up points of
15 distribution? No. We're going to have to do that
16 anyway, because among all the first responders, not
17 all of them will have kits or have access. Some
18 will have lost it. Some will have expired drugs.
19 So it's not going to prevent anything we're going
20 to have to do anyway.

21 Then I'm sitting back thinking what happens
22 when we then dispense millions of doses, and then

1 try to replace them every year, knowing that some
2 are lost and some are expired. And what's the cost
3 of that, in lies, because then the first thing we
4 do when we find out that the anthrax that's out
5 there happens to be doxycycline resistant, we have
6 all sorts of people who may be taking medication,
7 thinking they're protecting themselves when they
8 aren't and they aren't getting the message. And
9 then we still are responding and mobilizing, but
10 hopefully, we'll be bringing in the ciprofloxacin
11 and whatever other antibiotic might be appropriate
12 at a POD to distribute.

13 So because of the potential make things
14 worse and we're talking about dispensing millions
15 of doses per year, et cetera, how many lives are we
16 actually going to be saving?

17 If we look at the Russian experience, where
18 we have 1.2 million people, city, and a relatively
19 large release, among first responders, if we even
20 just talk about how many lives are we going to save
21 by providing these millions of doses to them, and
22 to their families, and to their children -- even

1 though there may have been only two pediatric cases
2 of inhalational anthrax recorded -- if we don't
3 have that number figured out or even estimated
4 through what we believe to be a reasonable model,
5 as weak as models are, I don't know how we could
6 move forward very well with any rationale
7 confidence that we're doing something of value to
8 society. We may actually be doing something quite
9 harmful.

10 DR. MOORE: Food for thought.

11 Dr. Gellad, you had a question?

12 DR. GELLAD: Thanks. I wanted to go back to
13 a point Dr. Reidenberg made. I guess I'm not fully
14 understanding. If all of the family members'
15 medication will be in the kit, how do we get at
16 this issue of prescribing to people who are not
17 your patients?

18 Because you brought that up, and I think
19 that's a really important point. Are they going to
20 go to different providers and the pharmacy's going
21 to put all of these in a bag? How is that going to
22 work?

1 Then if that is the case, then I think a
2 study is needed to determine the feasibility that
3 that can actually happen for family members.

4 DR. NEILL: Make more family doctors.

5 [Laughter.]

6 DR. GELLAD: That's a point well taken.

7 DR. MOORE: Dr. Erstad, you wanted to make
8 a -- respond to Dr. Gellad? I'm sorry.

9 DR. GRIFFIN: Marie Griffin.

10 DR. MOORE: Thank you.

11 DR. GRIFFIN: I just wanted to sort of agree
12 with some of the last comments, that this is
13 setting up a parallel that really I don't think
14 saves us from the national -- the national system
15 will essentially be the same. We're setting up a
16 parallel system for a specific group of people.
17 But among those people, it's probably only going to
18 be the people who can afford to do this or that
19 they're spending money they really can't afford to
20 do this every two to four years, it sounds like.

21 Then take that in the context of the IOM
22 report, where they specifically said having a kit

1 with one particular drug included would not be a
2 good idea because it's easy to make a resistant
3 anthrax strain. I think we would have to endorse
4 this with considerable caution. And I think,
5 really, there are a lot of downsides to it.

6 DR. MOORE: Okay. I'll do this. We'll take
7 a break five minutes early, and then we will come
8 back. We'll take a 15-minute break. I have to
9 state this here.

10 We will now take a short 15-minute break.
11 Committee members, please remember that there
12 should be no discussion of the meeting topic during
13 the break, amongst yourselves, or with any member
14 of the audience. We will resume at 3:10.

15 (Whereupon, a recess was taken.)

16 DR. MOORE: Ladies and gentlemen, we'll go
17 ahead and get started. If everybody could take
18 their seats, we'll get started. We have a limited
19 amount of time and we really have a lot to cover.

20 Now, we've had some very thoughtful comments
21 and a lot of good discussions so far, but I want to
22 try to focus our comments toward the questions at

1 hand.

2 So if I may, we'll just recap briefly the
3 first question. So as Dr. Laessig said, the FDA
4 would like us to comment on the public health
5 implications of the prescription doxycycline medkit
6 intended for post-exposure prophylaxis for an
7 anthrax counterterrorism event.

8 Specifically, I'd like the panel to address
9 the potential benefits and risks if a medkit were
10 approved with the intention of home storage. This
11 is the major question I think for today.

12 Here's the thing. I'm not going to be able
13 to -- because of the size of the panel and the time
14 left, if this were a voting panel, I would go
15 around the room and take everybody's vote. But
16 since it's not a voting question, and we don't
17 really have the time to do that, I'm going to ask
18 everybody to weigh in briefly with a comment, just
19 ad-lib, and we'll see how it goes. I may have to
20 enforce some rules a little bit later, but for now
21 we'll just let the statements begin. Fire away.

22 So for question 1, Dr. Neely, you're first.

1 DR. NEELY: So kind of taking an approach
2 like Dr. Curry did earlier, trying to step back a
3 little bit, I think in this country, we have made a
4 commitment and a decision that we restrict the
5 initiation and use of antibiotics to prescription
6 on a prescription basis only, with the exception,
7 perhaps, of some patients who chronically take
8 antibiotics or recurrently that we might, as
9 physicians, on an individual basis prescribe them
10 antibiotics. But on a public-scale basis, we
11 restrict it to prescription only.

12 I think we've all heard a lot of evidence or
13 at least opinion today. Perhaps, at least my take
14 it is that we are setting aside discussing
15 distributing antibiotics to the whole population
16 and considering just to a first responder group.

17 Then I think the question becomes, well,
18 what would giving home antibiotics to first
19 responders accomplish? And I think we have to step
20 back a little bit and think about what the role of
21 first responders is in this situation. And I think
22 one study that needs to be done would be to compare

1 and to find out what is the advantage of having a
2 first responder have antibiotics at home versus
3 getting it from a point of distribution just like
4 everybody else does, but perhaps they are first
5 responders because they get information earlier
6 than perhaps the general population would or some
7 other scenario. But I think that study is going to
8 be critical to determine whether or not there is
9 any point to going ahead with these med packs for
10 home use.

11 DR. MOORE: Thank you. I'll jump in here.
12 It hasn't really been specifically excluded. I
13 know we were talking about giving these medkits to
14 first responders, but it seems to have been implied
15 that there may be a role for general population
16 distribution later, which I think we can all agree.
17 And I think the evidence shows that would be, in my
18 opinion, a uniformly bad idea.

19 Specifically speaking to the public health
20 aspects, both of that as well as to the first
21 responders, as Dr. Parker mentioned, we really
22 don't know who the first responders we're talking

1 about. Some numbers have been thrown around, and,
2 really, I think 5 percent of the U.S. population at
3 its max is, in my opinion, really no better than
4 having general distribution, because you're really
5 talking about twofold problems.

6 There will be -- regardless of attempts
7 otherwise, you have to assume there's going to be
8 some unauthorized use. There has been unauthorized
9 use in some of the studies so far. You're talking
10 about -- I don't know what percentage of that.
11 We'll say 5 percent would engage in unauthorized
12 use. But there is that significant problem of
13 creating resistance, particularly with a class of
14 compounds which are becoming our last stand against
15 multi-drug-resistant gram negative bacteria and for
16 which there really are no other antibiotics on the
17 horizon. That to me is a major concern.

18 The other issue is -- and this is based on
19 my anecdotal experience back in Kansas in 2001.
20 Kansas has a significant number of tick-borne
21 diseases, Rocky Mountain spotted fever, Q fever,
22 tularemia, ehrlichiosis, anaplasmosis. And with

1 regularity, we would see cases every summer and
2 fall. And in the days following 9/11 and in the
3 anthrax attacks, we still had transmission of tick-
4 borne diseases in the early fall, late summer.

5 We couldn't get doxycycline because when the
6 cipro was all gone, people started hoarding
7 doxycycline. And we had people who were hoarding
8 doxycycline for a theoretical anthrax event to the
9 point where we couldn't give people who were
10 literally dying of tick-borne diseases actual
11 medication to treat them. And I'm very gravely
12 concerned about the public health impact being the
13 limitation, the drug shortage on doxycycline
14 nationally with this program.

15 I have to say, at the risk of limiting
16 access in an emergency, in my opinion, I fall on
17 the side of the argument that the pharmacies should
18 be the ones to dispense the medication because
19 they'll be able to instruct patients accordingly.
20 They'll be able to -- the pharmacists could educate
21 the patient taking it. Their medications will be
22 stored at a known temperature in a secure location.

1 This is not to say that first responders
2 can't be trusted with the medication. It's just
3 that there are a lot of other variables that were
4 mentioned earlier that I think would be best
5 used -- well, it would be best served to have a
6 control environment for the doxycycline.

7 That's all I'll say about that.

8 Anybody have any questions or any other
9 comments? Yes, Dr. Wolfe.

10 DR. WOLFE: This is really extending off of
11 what you just said, Dr. Moore, which is, if we are,
12 which I think is where the conversation is going,
13 in that direction, limiting the "medkits" or
14 whatever else to the first responders, then you're
15 essentially saying that 90, 95 percent of other
16 people will in fact get their tetracycline or
17 doxycycline at the POD.

18 If it's a public health decision made on the
19 basis of the best evidence at the time that there
20 is or appears to be an attack, the PODs are set up
21 to respond very, very quickly, and that's where
22 most people can get their drug. And if most people

1 can get it there, then the question remains why
2 can't the first responders also get it there? I
3 mean, the public health model -- I mean, the reason
4 why -- the question before, that Dr. Young asked,
5 is this precedent-setting. Yes. It is
6 precedent-setting. Again, it's precedent-setting
7 against the public health model, where public
8 health physicians, public health pharmacists are
9 there ready to give out something when there is
10 enough of a trigger to occasion it.

11 So I'm, again, arguing in the direction for
12 using entirely the public health model, the
13 predistribution, predispensing, before, well before
14 in many cases, anything happens. In the home, I'm
15 thinking less and less is a good idea.

16 DR. MOORE: Thank you.

17 Dr. Neill? Dr. Neill, go ahead.

18 DR. NEILL: I don't have a comment. They've
19 been mentioned.

20 DR. MOORE: Thank you. Dr. Day?

21 DR. DAY: On the slide, it does say to
22 comment specifically about potential benefits and

1 risks. We've heard a lot about risks today, and
2 there are plenty in the briefing materials. I'd
3 like to raise the possibility of one in addition.

4 So many of the materials to be provided in
5 medkits in the future and that have been provided
6 in the studies in the past involve the crush-and-
7 mix procedures. Now, nobody mentioned, when
8 someone gets a household kit, whether those
9 procedures would be in there even if they don't
10 have kids at home or if they don't have any adults
11 who have problems swallowing.

12 So even so, there'll be some information
13 about it. When you open up the kit, one of the
14 things that I think the public or the first
15 responders would see would be that syringe. Oh,
16 what do I do with this, and so on, and getting into
17 all the procedures for doing it.

18 So I think that there would be an increase
19 in the number of people who would do the crush and
20 mix, and put it in pudding, or whatever, and ingest
21 it than need to. And the more times that's done,
22 there's a greater exposure for potential error,

1 either overdosing or underdosing, both of which
2 would not be so good.

3 So even when the materials would be very
4 clear, that little booklet that we saw today, the
5 one-page, it looks like a booklet, with the
6 instructions about how to crush and mix, et cetera,
7 even if that's very good, and if it tests pretty
8 well, 85 percent comprehension, or 90, or whatever
9 it is, under duress, other things can happen.

10 I often test patients in my laboratory, but
11 I've also tested some of the best and brightest
12 people in the country, very bright, quick
13 undergraduates at Stanford, and at Yale, and at
14 Duke, and at Carnegie Mellon, and to speed up a
15 task a little bit, which kind of simulates stress,
16 they make a lot of errors.

17 So this is a potential risk that if there is
18 a need to take one form and translate it into
19 another form, that the dosing will be incorrect.
20 So if these were to go forward -- and I do have
21 reservations about that -- I would want to
22 seriously consider different formulations in the

1 bag, so the tablets for the adults, and maybe the
2 liquid for the kids, and so on.

3 I know there's problems with expiration and
4 all that kind of thing, but I don't think the
5 materials are distinctive enough yet. The self-
6 selection isn't easy to find. There's three
7 categories of people. You take the tablet, you
8 crush and mix, or you don't take anything. And
9 it's very hard wading through all of these things
10 right now, and so there are risks for all the
11 categories of people.

12 DR. MOORE: Thank you. Dr. Ockenhouse,
13 you're next.

14 DR. OCKENHOUSE: Thank you, Mr. Chairman.

15 I am going to speak in my capacity as a
16 patient representative and not as an infectious
17 diseases physician. I value all the opinions here
18 today. I have utmost confidence that first
19 responders and their families can take the
20 medication as indicated, or the prophylaxis, for a
21 catastrophic anthrax exposure.

22 First responders, by their very nature and

1 job, are sacrificial in what they do. And for them
2 to know that their families are taken care of in a
3 time of national emergency is a great thing to
4 provide them. I'm also aware that this program for
5 prophylaxis for first responders may metamorph into
6 something larger is problematic, and I would limit
7 my support as a patient representative for this
8 particular group.

9 Also, on the side, I'm also a member of the
10 military, which has seen and used millions of doses
11 of doxycycline throughout the world in a safe
12 manner without the evolution of resistance. I'm
13 actually more concerned not that there will be
14 overuse, but there will be underuse of doxycycline
15 because of the toxicity or the tolerance -- not so
16 much the toxicity, the tolerance that it may
17 provide.

18 So as a patient representative, I see very
19 little downside in that I would recommend that
20 there should be an exemption made that further
21 studies would be studied to look -- to examine the
22 unauthorized use of doxycycline.

1 Now, having said that, I also feel very
2 strongly about the equity. And part of the equity
3 is why should the family members of first
4 responders have to pay for something when it's
5 going to be distributed in a biologic, catastrophic
6 event free to the rest of the population?

7 Now, first responders themselves, by their
8 health plans or by their negotiated union
9 agreements, may be provided the doxycycline free.
10 This may not extend to the family. And I would
11 think that on the basis of equity alone, that idea
12 of cost should be reconsidered. Thank you.

13 DR. MOORE: Thank you. Dr. Parker?

14 DR. PARKER: So I would reiterate some of
15 the comments that there are certainly many risks.
16 And it's hard for me to define what the benefits
17 are, period. Short sentence.

18 The other question I have is whether or not
19 moving forward would actually create harm, and I
20 think that's really worth consideration. I think
21 moving forward with the medkits and making them
22 available to either first responders or the general

1 public carries with it a message of fear. And I
2 would ask us whether or not that's warranted and
3 whether or not, as a public health agency, that is
4 the message that we intend, with the possibility
5 that that can be perceived. And I think that's
6 incredibly important to consider.

7 With a message of fear also goes concern
8 about equity, and about justice, and about
9 security, and whether or not there is the
10 possibility that by moving forward, we actually are
11 presenting to the public the best evidence about
12 our own security.

13 DR. MOORE: Thanks.

14 Dr. Cappelletty?

15 Dr. Kaplan, you're next. Sorry.

16 DR. CAPPELLETY: Again, looking at trying
17 to assess the benefit, it is I think extremely
18 unlikely if somebody's going to use this as a
19 bioterrorism weapon, that they're going to put a
20 fully susceptible strain out in the environment.
21 So the likelihood of a bioengineered product is
22 very likely making, I think, any antibiotic that I

1 think would go out there a fairly moot point. And
2 so to try to weigh the risk versus benefit when
3 that unknown is out there is a little bit difficult
4 to do.

5 I also question again the issue of
6 awareness, concern, or panic regarding one of these
7 attacks; is it warranted? I think back to the H1N1
8 when it started a couple years ago, and the
9 heightened awareness, and the push forward, and
10 then it never came to be. And so the public just
11 looks at the system as, there you go again crying
12 wolf, and nothing is the end result of that.

13 So if we do that again on this level, are we
14 just going to be crying wolf yet again where the
15 masses are concerned, and they're going to dismiss
16 anything in the long run with that anyway.

17 DR. MOORE: Thank you. Dr. Kaplan?

18 DR. KAPLAN: I guess I'm coming down on the
19 side of the first responders in terms of being very
20 sympathetic to their thoughts and their families.
21 And not having necessarily been a first responder
22 myself, but I see what goes on, let's say during

1 disasters in the Houston area with hurricanes and
2 the decisions you have to make about being on call
3 and leaving your family.

4 But I think there can be probably a
5 modification. I mean, I really do like having
6 first responders being able to get their
7 medication, this medkit perhaps, but not having it
8 ahead of time at home, being the very first people
9 that can get it at the very first sign. Because I
10 know what's going to happen. I mean, you say you
11 can go to a POD, but the traffic is going to be
12 unbelievable.

13 We had an issue in Houston several years ago
14 where people were asked to leave the city, and you
15 couldn't leave the city. It was pandemonium. You
16 could get 15 minutes away from your house, and that
17 was about it. I see the same thing happening with
18 these PODs.

19 So whether or not each local government,
20 state, and city authorities can come up with an
21 identification of who's the first
22 responder -- that's what we have on our badges so

1 that you can get through into the medical center if
2 you're on call and you're the person for these
3 disasters.

4 DR. MOORE: Thank you. Dr. Landis?

5 MS. LANDIS: Originally, when I had looked
6 at this information, I thought, "Oh, gee, the fact
7 of putting a kit in the house sounded like
8 something that I would not agree with." But having
9 thought about it a lot more, I think it is the
10 first step in emergency preparedness. I think that
11 with proper education -- and I'm not real set on
12 that medkit that's in front of us. I think that
13 there's a lot of work that needs to be done to make
14 it more appropriate and user friendly.

15 If there is transparency to the population
16 as far as the need for additional security for
17 individuals, I think that there would be an
18 understanding of why first responders would be
19 those that would already have it. And you talk
20 about that 5 percent of the population. The
21 reality is, a very small part of that 5 percent of
22 the population would actually have to utilize that

1 if there was an outbreak, because we're talking
2 about 5 percent maybe across the U.S. It would
3 probably be just a small area that we'd be looking
4 at. So that kind of drills it down even more.

5 I think we need to enable people. We need
6 to educate them. If we don't do this -- this is
7 all very public. People can go on the internet.
8 They can see this. I can see people getting
9 prescriptions from their physicians. "I'm just
10 going to get my 10 days of doxycycline or my
11 60 days. I'm going to have it on hand now,"
12 because that's the mentality. I think the more
13 open we are, the more transparent, and letting them
14 know why we're doing this, and the direction that
15 we're going in, I think will enable people to make
16 better decisions. I think that if they're
17 educated, that they would not be getting into these
18 kits, that there would be a better understanding of
19 it.

20 DR. MOORE: Thanks. Dr. Woods?

21 DR. WOODS: Thank you. I have great
22 appreciation for the first responder perspective,

1 having a brother who's a first responder. However,
2 to me, this seems to be more of a system issue than
3 a packaging issue. In response to Dr. Kaplan,
4 you're right. It will be pandemonium getting to
5 the PODs. But are there ways for us to develop
6 systems where maybe we take some of the contents of
7 the PODs to a place where first responders
8 congregate?

9 I think there are ways to figure this out,
10 short of creating a whole new set of packaging,
11 which leads me to the packaging issue. And I'm not
12 buying it. I personally don't see what having it
13 in a baggie is going to do to prevent people from
14 using doxycycline inappropriately if they want to
15 use doxycycline inappropriately. I just don't
16 think we've got data to suggest that that's going
17 to prevent people from doing that. I think, if
18 we're going to develop more time and energy to
19 studying that, we need to really examine that
20 issue.

21 I also think, with respect to the family
22 issue -- again, I have great compassion for the

1 first responders wanting to ensure their families
2 are safe. I think that's what all of us would
3 want. However, I think making the contents of
4 these packets available to families in a way kind
5 of perpetuates the misconceptions about the way
6 this disease moves. And I guess I would go with
7 what Dr. Landis said. I think there's a real
8 educational opportunity here to help people better
9 understand how this moves, short of just providing
10 the family members medication irrespective of their
11 exposure.

12 Finally, this whole issue of public versus
13 individual stockpiling, to me, as I kind of think
14 that through, by encouraging individual
15 stockpiling, that probably makes our assessment of
16 inventory and our capacity to treat people more
17 unpredictable rather than more predictable.

18 So I guess, as I think all that through, I
19 would lean probably against the packet concept and
20 really maybe encourage looking at our existing
21 systems in ways we could perhaps optimize those.

22 DR. MOORE: Thanks. Dr. Reidenberg?

1 DR. REIDENBERG: Yes. In thinking about the
2 urgency of this, ever since the anthrax attacks,
3 people have known that cipro and doxy work. And
4 anybody who wants to could go to their prescriber,
5 and get prescriptions and have a stockpile in their
6 home right then.

7 So one research question is to find out how
8 many people perceive this as enough of a problem to
9 have actually purchased doxy or cipro and had it
10 available for the next anthrax attack. If the
11 number is small, then we're not talking about
12 making a medical kit. We're talking about creating
13 a whole advertising campaign to create a need. And
14 I think that we need to think very seriously
15 whether our goal is to create a need in order to
16 get home stockpiles or whether that really isn't
17 our goal.

18 DR. MOORE: Thank you. Dr. Morrato?

19 DR. MORRATO: Yes. I don't want to repeat
20 what others have said. I had many agreements with
21 what Dr. Woods and Dr. Kaplan said. I just want to
22 say, though, that whatever decision is made, I

1 think we need to make sure that it's consistent
2 with whatever the postal worker program is because
3 that's going on in which the product is out in
4 families, in homes, and that community of workers.
5 And it doesn't seem, to me, logical why that would
6 continue whereas the medical first responders
7 wouldn't. So whatever gets decided, I think those
8 two programs need to be in synergy with one
9 another.

10 DR. MOORE: Thank you. Ms. Young?

11 MS. YOUNG: I agree with the last few
12 comments. I think we do have to protect our first
13 responders. I hope there are other ways to do it.
14 And I would encourage the defense agencies to be
15 looking into that. Some of the ideas that came up
16 here are good, a more targeted approach, not
17 setting the precedent of providing the whole
18 population with various countermeasure agents. I
19 think that is something that could set a precedent.

20 Also, I'm concerned about, in the case of a
21 real emergency, the panic effect of people who want
22 these kits, and don't have them, and what might be

1 done in terms of pressuring public health agencies,
2 or pandemonium, and such. And also, if there's a
3 resistant agent out there and people are using the
4 kits that are in-house and they're not working, the
5 psychological effects of that. Also, use by the
6 elderly, a growing population of Alzheimer's
7 patients, low literacy, and our transitional
8 patients in the inner city, all kinds of
9 transitional communities and populations that
10 really don't fit the model of a nice, neat
11 household.

12 So those are my concerns.

13 DR. MOORE: Thank you. I believe that's it
14 for now.

15 Yes. I'm sorry. Dr. Gellad?

16 DR. GELLAD: I'll just say one thing, and
17 I've spoken enough about some of the risks. I
18 think what makes it very difficult to address the
19 potential benefits is the benefit is directly
20 related to the risk of an anthrax attack. And I
21 don't want to know. I'm sure someone does. But I
22 think I'll just make the point that that's what

1 makes it difficult. If you told us there was a
2 95 percent chance an anthrax is going to happen in
3 the next week, I think that completely changes what
4 we're talking about. And so that's the difficulty
5 I'm having in thinking about the benefits of this
6 thing.

7 DR. MOORE: I'll have to agree. I think
8 that's the difficulty we're all wrestling with.
9 The whole issue, the same issue, is with the
10 smallpox vaccine. I mean, should we give a vaccine
11 for a disease that doesn't exist anymore? If the
12 risk of getting a vaccine is .1 percent death, then
13 that's unethical if you're giving the vaccine for a
14 disease that doesn't exist.

15 So it's the unknowable that's impossible to
16 nail down. And that's really the -- I agree with
17 you completely. That's the qualifying information
18 we really need to make a recommendation to the FDA.
19 And yet, that's the information that can't be
20 known.

21 Yes. Dr. Curry?

22 DR. CURRY: Yes. I would just say that if

1 we thought there was a 95 percent chance of an
2 anthrax attack in the next week, we'd probably be
3 setting up PODs with numerous antibiotics, not
4 knowing which one we would be using.

5 DR. MOORE: I would be hiding in the
6 basement somewhere.

7 So with that, let's move on, then, to the
8 second question. Part A, please comment on
9 additions or modifications to the proposed and/or
10 completed studies, e.g., label comprehension,
11 palatability, simulated use, or additional studies
12 that would help to assess the risks and benefits.

13 What types of additional studies would be
14 helpful to assess how users would behave in a real-
15 life situation? And we'll go ahead and ask the
16 next question, which is, what is a reasonable
17 percentage of study subjects who should understand
18 the various components of a label and/or be able to
19 refrain from using the product for other purposes?

20 Dr. Neill?

21 DR. NEILL: So there are already available
22 medications on the market that in one respect or

1 another fit the model that we're talking about for
2 medkits in first responder use. And the examples
3 that came to mind in my quick thinking include
4 valacyclovir for recurrent HSV infection, EpiPens
5 that people carry around, hopefully that still work
6 when they get anaphylaxis, cipro that, on the CDC
7 website, still exists as something you might ask
8 your doctor for to prevent traveler's diarrhea.
9 There are others.

10 Now, traveler's diarrhea is not anthrax, but
11 this concept that there's this method which
12 involves a one-on-one physician-to-patient
13 prescription for the patient to fill at a pharmacy
14 using the standard market methods -- I'm sorry. I
15 said there was a method -- the standard mechanism
16 for getting the med into the home for use at some
17 appropriate time later exists out there.

18 I feel like the sponsor -- I have to point
19 out, having been on the committee off and on many
20 years, this is the first time there's been a
21 non-industry sponsor, and it's a government
22 sponsor. This is fascinating to me.

1 The sponsor seems to be asking not whether
2 or not having this antibiotic in the hands of
3 people exposed is a good idea or whether there's a
4 mechanism for doing that. There is. It already
5 exists. It's legal. People call me up. They make
6 an appointment. They send us a phone -- something.
7 They stop you in the hall and say, "Give me some of
8 this." And we've heard some docs suggest that that
9 happens now, and it does, and it will continue.

10 But whether or not what they're proposing is
11 an improvement or not -- and I won't reiterate all
12 the issues. I think the committee has done a
13 really good job of pointing out the risks to the
14 public health infrastructure, et cetera, and
15 relying on this one-on-one response to what is a
16 public health issue, and all of the uncertainty
17 inherent in an action that occurs distant from the
18 intended response later on down the road.

19 Having said that, I wanted to give that
20 context because my sense is that the questions that
21 we're being asked to focus on are actually much
22 more limited, given what's already available in

1 terms of response. And given that I'm on the
2 Nonprescription Drugs Advisory Committee, I hear
3 these questions in my OTC mind in terms of label
4 comprehension, et cetera.

5 To speak specifically to this question 2A
6 and B, the kind of studies that have already been
7 started do not include an actual-use study or a
8 label comprehension study, which is more than
9 "Answer this fill-in-the-blank question or
10 multiple-choice question correctly. Did you
11 understand?"

12 Rather what ought to occur, show people a
13 box in whatever setting you're going to show,
14 hopefully as realistic as possible, and not for
15 this purpose, in the midst of an anthrax attack.
16 But you'd show it to them, and then eight months
17 later, show up one day at 2:00 in the morning. And
18 knock on the door and say, "Okay. It's time. Use
19 this." Then watch what they do. And if they do it
20 correctly, they comprehend it, and things work
21 fine -- they don't have to take the medicine. But
22 I would suggest that as a study, that would be

1 helpful in informing me about whether or not there
2 ought to be changes to the label, the method, the
3 compounding, et cetera, if you really wanted to
4 have some effect for these folks to get out of bed
5 and go first respond.

6 In terms of other studies, this is one area
7 where, because it would be unethical to release
8 anthrax in a randomized way and see how things
9 happen, it's really imperative that, in addition to
10 label comprehension, and actual use, and all these
11 kind of usual studies, that there be attention paid
12 to the historical record. The AMA representative
13 earlier mentioned Sverdlovsk in Russia. And not
14 that I didn't pay attention to every single word
15 said earlier, but I did read through that entire
16 primary paper to see what in the heck happened
17 there. Fascinating story.

18 There are other corollaries that inform the
19 behavior of populations, both the first responders,
20 the patients in the exposed area -- for example,
21 Three Mile Island in Harrisburg in 1976, there has
22 been mention already about potassium iodide

1 distribution around nuclear power plants. That
2 already happened. That's I think a reasonable
3 model to look at.

4 Meningitis outbreaks in Philadelphia in the
5 last several years, there have been several cases
6 that have involved what I would characterize as
7 hysteria and the sort of mass rushing for
8 antibiotics, et cetera, some of it appropriate,
9 much of it not. But there is I think very
10 informative data that could be used to inform this
11 question: Do you give medicine to people six, and
12 eight months, or a year ahead of when they might
13 otherwise have to use it based on what we know
14 about how people behave in an acute, urgent,
15 hysteria-inducing situation?

16 So I'll reserve other comments for the other
17 questions.

18 DR. MOORE: Thank you. I guess I would echo
19 those salient remarks by saying it'd be nice to
20 know what the potassium iodide tablet use was in
21 California.

22 DR. NEILL: 130-milligram packets

1 distributed in Ocean County in New Jersey. And
2 they're available through the county health
3 department. You have to go several layers deep in
4 the website. Again, not that I didn't pay
5 attention to everything that was being said.

6 DR. MOORE: What I'm saying is it would be
7 nice to know what the pattern of emergency use was
8 for those pills after the Japanese tsunami when
9 there was discussion about contamination and there
10 was a rush on potassium iodide. If we want to look
11 at more current use in households, it'd be nice to
12 get that information. And I don't know if that
13 information is knowable, but that's to me very
14 helpful.

15 I will say this. The information regarding
16 the prepositioning of Tamiflu -- was the
17 prepositioning of Tamiflu done before the recent
18 avian flu outbreak or was that afterwards? Do you
19 guys know? Does the FDA know?

20 It was before. So the question really was,
21 then, it'd be nice to know what the personal use
22 was of Tamiflu in that situation.

1 DR. KORCH: Are you talking about Tamiflu in
2 the state of caches or provision of Tamiflu once
3 released from the Strategic National Stockpile
4 after identification of H1N1? I mean, that's two
5 different --

6 DR. MOORE: Well, perhaps I misunderstood.
7 What I was wondering was, was Tamiflu prepositioned
8 to first responders or to other local agencies
9 prior to H1N1, and then what's the pattern of use?
10 So it was not prepositioned to localities or
11 individuals.

12 DR. KORCH: Tamiflu was prepositioned to
13 states.

14 DR. MOORE: Right. Never mind.

15 So that's, to me, the issue. That's a
16 source for additional data.

17 I guess the other thing, as Dr. Neill was
18 saying, is it's hard to recreate the scenario by
19 which you realistically understand and assess how
20 people use those kits, short of having them be
21 five feet away from a pit-bull on a four-foot
22 chain.

1 It'd be really difficult to try to recreate
2 some situation where there is some fear of an
3 outbreak, although I'm not sure that knocking on
4 the door at 2:00 in the morning is the best idea.
5 You're liable to get shot.

6 Dr. Parker?

7 DR. PARKER: I might just comment. We did
8 have a piece in the New England Journal with the
9 use of oseltamivir and the EUA that was put out on
10 using it, the dosing problems that had to do with
11 the included syringe, mass units versus volumetric
12 measurements that came out, labeling requirements,
13 how incredibly complex it is. And in doing that,
14 it was very clear that compounding is not a task
15 that is even familiar to all pharmacists because
16 it's not done that commonly.

17 I'm not sure I could find anyone that I work
18 with, including the physicians, who could probably
19 completely follow those instructions and do them
20 accurately, all the way down to reconstituting with
21 the water. And then it doesn't tell you on the
22 front, by the way, that you need a teaspoon to add

1 those three teaspoonfuls of water to the solution
2 that you've then created, that was made with the
3 apple juice, or the chocolate milk, or whatever the
4 third thing was.

5 You then add three teaspoonfuls of water,
6 and then you dose that. And the final picture on
7 the back of that shows a child with a spoon or a
8 syringe. So you then redraw it up in the syringe
9 or you put it back in the spoon, and you give this
10 child at least three and a half teaspoonfuls or
11 however many mLs.

12 It's so incredibly complicated when you get
13 down to what the actual task is in delivering. You
14 get down to, how much does it matter if you deliver
15 the right amount? What's underneath what it really
16 requires? So I have tremendous problems with it.

17 The good thing is -- I thought about the
18 benefit -- this highlights how incredibly hard it
19 is to accurately take medications.

20 DR. MOORE: Good point. Dr. Vaida?

21 DR. VAIDA: Yes. I think a lot of these
22 studies that we did read are very good. And even

1 with the first comments on drilling down even a
2 little bit deeper would be great for any of the
3 medications, regardless of even this study. We'd
4 love to see that, our organization.

5 But I think, in the bigger picture, after
6 hearing all the discussion with number 1, I think
7 if you're going to put more resources and dollars,
8 it should be in looking at how to distribute the
9 medication out quicker, the stockpiling, where that
10 should be done, how it should be done, the points
11 of distribution, and how you could get it out to
12 the first responders. I just think that any
13 resources and money after what we all talked about
14 here, that's what you should really be studying
15 right now.

16 DR. MOORE: Thank you. Dr. Fischhoff?

17 DR. FISCHHOFF: I'll follow on that. I'll
18 suggest two analytical studies and two behavioral
19 studies. The analytical one, one would be trying
20 to model the distribution of the drug under
21 different scenarios, using operations research,
22 operations management methods, but with

1 behaviorally realistic assumptions. The
2 challenging problem, if you can't figure it out,
3 then you ought to know that we have a system that
4 we don't understand.

5 Secondly, we ought to do the same kind of
6 analytical work about the distribution of adequate
7 information to the heterogeneous populations that
8 we're interested in. There's often in
9 communication circles a lot of hand-waving about
10 social media, and partners, and this, and that.
11 But we need to know what percentage of people will
12 get the information that they need, be able to
13 access, and be able to act on it so that we have an
14 estimate of whether people get the stuff and then
15 whether people can actually use it.

16 Those would provide the parameter estimates
17 with which one could begin to answer the second
18 question there, which is, is this good enough for
19 us? I suggest that as input to our leadership,
20 there are two kinds of behavioral evidence that we
21 collect. One is the structured consultations with
22 diverse members of our society about what they

1 think about the fundamental principles, the
2 philosophical, political, social contract
3 principles that underlie these different programs,
4 in terms of whether individuals are responsible for
5 themselves or government is assuming
6 responsibility.

7 Talk to people. We can give you our
8 insights on what they think, but talk to them.
9 You'll get a diversity of opinion, but you may also
10 get some clever suggestions about how to design and
11 position the program.

12 Second is that, based on those analyses, one
13 can anticipate stuff that's going to happen, that
14 there will be missed doses. There will be
15 coincidental hot spots of other diseases that are
16 unrelated -- side effects that are unrelated to
17 this. We should have prepositioned an inventory of
18 communications that are scientifically valid,
19 empirically tested, in order to be able to address
20 those concerns. We're routinely caught
21 flat-footed. We routinely shoot ourselves in the
22 foot by being unprepared for completely predictable

1 classes of surprises.

2 I think the gambles we want to take here are
3 gambles of this is our national security policy.
4 This should be made at the highest level. We're
5 making a very strong statement here, and the kind
6 of information that our leaders need to know is
7 what kind of public acceptance there will be for
8 the best-designed program, which will have the best
9 possible distribution, the best possible
10 communication about usage, and the best possible
11 communication about incidents that arise.

12 DR. MOORE: Thank you. Dr. Neely?

13 DR. NEILL: I'm okay.

14 DR. MOORE: Dr. Walker?

15 DR. WALKER-HARDING: In terms of looking at
16 any study that's done that has to do with how well
17 people use things, how well they read the label, I
18 would make the suggestion that it goes down to
19 age 12. And anybody age 12 and older should be
20 able to follow these directions.

21 Specifically dealing with people who are
22 first responders, who could be the people that have

1 to dispense the medications at the PODs, they may
2 be single parents and the oldest person in the home
3 may be 12 and may be the one giving the meds to the
4 other family members.

5 A kid 12 years old can take their own
6 medication, but it would be important to make sure
7 that they know how to do this as well. So if there
8 are any tests that are done on how well people read
9 and comprehend and follow the directions in real
10 life taking it, we should go down to age 12, not
11 just start at 18.

12 DR. MOORE: Thank you. Ms. Landis?

13 MS. LANDIS: Yes. Just listening to
14 conversations, I really haven't heard anybody say
15 that, "I love the kit the way it is."

16 [Laughter.]

17 MS. LANDIS: Everybody's been picking away
18 at it all day today. And I would like to see maybe
19 some focus groups put together to really take a
20 closer look at this kit. Let's bring in some
21 pharmacists and have them utilize -- because
22 they're on the front lines, they're working with

1 patients every day, and they have a really good
2 sense of what flies and what doesn't fly. But have
3 them sit down and come up with what makes the most
4 sense to put in a kit as far as the education and
5 how you dose for peds.

6 Then maybe do some focus groups with just
7 the general population and see, does that make
8 sense, before you start to do any studies at all.
9 I think we need to refine the product first and
10 have it be the best possible before you start
11 running studies on it because then we're just kind
12 of kicking ourselves.

13 As far as the PODs, to me, it makes sense to
14 have your local pharmacy be the PODs, because where
15 else are you going to find a medication-use profile
16 for patients? So if anybody is going to be
17 screening, doesn't it make sense to have the
18 pharmacist be there to be able to evaluate what's
19 going on with a patient? A lot of patients don't
20 see one physician. They see three or four
21 physicians and urgent care. It's amazing what you
22 see out there. And I know that you all have an

1 understanding of that.

2 So somehow including a pharmacist to help
3 monitor is this the right medication for that
4 individual. We're the ones on the frontlines. We
5 can help with the process. And now with electronic
6 prescribing, it's so much easier for us to message
7 back to the physician so that they know this is
8 what's going on. And not in the case of first
9 responders when you're talking about prescription,
10 but if you're talking about the general population,
11 we have the ability to get that information back to
12 the physicians so that they know what's going on.

13 DR. MOORE: Thank you. Dr. Day?

14 DR. DAY: It's not only what types of
15 studies, but how they're conducted. So if there
16 are label comprehension and/or actual-use studies,
17 looking at a variety of different paradigms or ways
18 of testing would be useful. There's always an
19 emphasis on a questionnaire. You ask a question.
20 You get an answer. Move onto the next one. Or
21 say, "Why did you say that?"

22 There are a variety of cognitive paradigms

1 that have been around for over half a century,
2 where you get different types of
3 information -- levels of reporting for the same
4 information. So you could ask, say, about side
5 effects, and you could ask a free-recall type
6 of -- you could have a free-recall type of paradigm
7 where you just say, what are the possible side
8 effects of this drug, or allergic reactions, or
9 whatever you're testing. And then you have more of
10 a cued recall situation, where you just give one
11 and say, "Is this a possible one or not?" You
12 could have recognitions.

13 There are different levels of knowing. So
14 if there are some key messages that you want to
15 ensure that people have, don't ask once, and ask
16 why, and move on. But there are levels of knowing,
17 and those need to be tapped at those different
18 levels.

19 Another point to pick up on what someone
20 said over here, I was going to recommend that there
21 be studies where people read the materials and then
22 they're tested, but you vary the delay from the

1 time of reading to the time of test to see what is
2 retained. That often tells you what people really
3 did understand and then what remains at the top of
4 their cognitive deck, so to speak.

5 Then the final point is that, in doing label
6 comprehension, you can kind of simulate, not
7 entirely, the waking-up at 4:00 a.m. situation,
8 where you have the same testing program with the
9 different cognitive paradigms, let's say. But
10 there's a control condition where it's just study
11 and test, and another condition where it's speeded.
12 And you could speed up the amount of time that they
13 have to read the materials, which is probably
14 what's going to happen in the real world. "Oh, my
15 gosh, there's anthrax. Let me see. What's this?
16 What's this? Okay. Done."

17 So they may read more quickly. So what
18 happens when people read more quickly? There can
19 be a speeded study condition. There can be a
20 speeded test condition, where you only have a
21 certain amount of time to answer each because,
22 maybe in your household, there's a lot going on,

1 and you're answering, and doing things, and so on.
2 And you can combine the two, so there could be a
3 condition where both are speeded.

4 Then the last part that gets a little bit
5 more about what might be going on in a household
6 would be to do a divided attention task where, as
7 you are answering the questions and/or studying
8 them, you have to do another task at the same time.
9 And typically, in the lab, there are dull things,
10 where every time you hear a certain kind of word,
11 you tap a pen or something like that. But it could
12 be a baby cry or it could be something a little
13 more realistic so that if you can divide people's
14 attention in different ways, you can see what
15 they're able to know and do.

16 So if this goes forward with more testing, I
17 urge that the people doing these things take into
18 account what is known about how you test, not just
19 what you test.

20 DR. MOORE: Thank you. Dr. Morrato?

21 DR. MORRATO: Thank you very much. I wanted
22 to add to what Dr. Landis said because I had the

1 exact same thought, whether it be focus
2 groups -- also another methodology is to create an
3 expert panel in which it's comprised of the target
4 population. And they work with you iteratively as
5 you are mocking up, and developing prototypes, and
6 testing.

7 I would add as part of that qualitative
8 research an understanding of what are current
9 accepted beliefs, knowledge, and attitudes around
10 doxycycline or around anthrax, such that the
11 messaging on the materials can be addressing what
12 are common understandings, myths, fact, et cetera.

13 I might think about formatting it in a way
14 that people already have been trained somewhat to
15 look at medicines. You could look at the OTC kind
16 of labeling. A lot of work went into that as a
17 formatting way of approaching the information
18 quickly and easily accessible.

19 I might also consider building in, as part
20 of your development, someone that comes from the
21 OTC product industry. They have to create
22 labeling. They have to create materials and they

1 have a lot of, I bet, a wealth of knowledge that
2 could be brought to this. But clearly, it needs to
3 be tested before it goes quantitative again, would
4 be my suggestion.

5 Then in terms of the quantitative testing,
6 just adding on what others have said, I think it
7 was brought up earlier there should be
8 consideration of seasonal effects depending on the
9 duration of the study. I would also say maybe some
10 regional diversification. Not everyone has Lyme
11 disease, the same considerations across the
12 country. And so depending on what part of the
13 country, they might be more sensitized to using
14 doxycycline for different needs.

15 In terms of additional study, it was
16 mentioned earlier this morning about dosing for
17 children, and I would agree. I'm a parent, and I
18 don't know how much my kids weigh. And you might
19 consider, for that kind of study when you're
20 looking at the compounding in that, a simulated
21 use, doing it in pairs or somehow bringing it into
22 the fact of families with children, and what is the

1 actual weight and age of the child, and how good
2 did the parent approximate that, and make sure you
3 have moms and dads to the point raised earlier.

4 Then, my last thing to say relates to
5 point B, which we were supposed to give you advice
6 on a reasonable percentage of I guess success
7 criteria or what. And I don't think I should go as
8 low as 70 percent, which you mentioned earlier. I
9 don't think it has to be 100 percent, either. I
10 think we're looking at a population that I would
11 expect very high knowledge. And so I would expect
12 over 90 percent that should be on key goals,
13 whether it be on knowledge, or behaviors, or
14 whatever. But that I think should be attainable,
15 given the population that it's being focused
16 around. Thank you.

17 DR. MOORE: Thank you. Dr. Gellad?

18 DR. GELLAD: I had a couple thoughts related
19 to, I guess, outstanding questions I still had in
20 terms of future studies. The first was whether the
21 products for adults and children, or adults who
22 can't swallow pills, whether they have to be in the

1 same medkit and whether there was any thought about
2 creating pediatric medkits and adult medkits or
3 liquid medkits and tab medkits. That decision may
4 have already been made, but if not, that might be
5 one way to test whether separating out these
6 products will get around this issue of people won't
7 know what to do with the syringe when they get this
8 medkit.

9 The other thought was, there was a comment
10 in the material that the effective storage
11 conditions is still not known. I wouldn't know,
12 for example, if my patient told me they left it out
13 in their car overnight, in the cold for example,
14 what does that do. Do they need a new kit? Are
15 they going to know what to do with the kit at that
16 time if it's been subjected to abnormal conditions?

17 The other thought would be, we keep hearing
18 about the target populations, and we've devised
19 some ways to get larger samples of whatever target
20 population you're interested in, whether it's
21 minority or the occupational groups you're
22 interested in. And there are ways to get larger,

1 national samples that would probably be useful.

2 DR. MOORE: Thanks. Dr. Huntley?

3 DR. HUNTLEY-FENNER: So I just wanted to
4 say, there's no question that I think the first
5 responders should be a primary target of
6 prepositioning, whether it's at home or at special
7 points of distribution. I tend to lean toward the
8 latter. And there's no question that they could
9 and should be able to follow instructions. I think
10 Dr. Morrato is correct. You expect to find a
11 relatively high rate of comprehension or whatever
12 your measure of compliance is.

13 I do think that we ought to consider, as
14 we're preparing study participants with scenarios,
15 probably a couple of very different types of
16 scenarios. One would be relatively low tech.
17 You've got an engineered product with a low-tech
18 delivery system, highly localized, and another
19 that's fairly high tech, highly engineered, and
20 much more broadly distributed, more of a sort of
21 military scale.

22 I think those are fairly different

1 scenarios. You may find that the perceived risk to
2 individuals who are approximate to the geographic
3 target might vary significantly depending on those
4 two types of scenarios.

5 I wanted to just reiterate Dr. Curry's point
6 about, well, if we knew an attack was going to
7 happen next week, we would likely want to
8 preposition PODs with multiple antibiotics because
9 we wouldn't necessarily know what sort of strain
10 we're looking at. I think ideally we probably
11 would not have to choose between, let's say, cipro
12 and doxy. We probably might go with both or maybe
13 even a third option.

14 Regarding the study themselves, I do think
15 we ought to be thinking about where breakdowns are
16 likely in comprehension, or in decision making, or
17 behavior compliances are likely to occur. And
18 these may vary by occupation, by linguistic status,
19 by whatever subpopulation of first responders or
20 their family members that we're thinking about. So
21 we'll want to have a strategic idea about where
22 those weak points are and make sure that they're

1 covered closely in the study.

2 I obviously wanted to focus very closely on
3 the pediatric dosing issue, and I'm sure we'll get
4 to that in question 3.

5 I do think we're talking about a process
6 here that's not just a one-stage process. So for
7 example, we may want to consider, once we
8 prepositioned kits, following up. We're talking
9 about a 60-day course, ultimately. We know that
10 the kits are 10 days. And we're going to have to
11 make decisions about where to begin the follow-up
12 to complete the 60 days. And so we'll need to have
13 some way of folks maybe reporting in that they've
14 begun treatment, and that they've done it
15 correctly, and et cetera, how many people have been
16 treated.

17 We'll want to consider also the issue that
18 first responders may be selfless. If they can't
19 use -- if they don't have enough medication for
20 their families, for themselves and their families,
21 they might actually give it to their families and
22 not use it themselves. There obviously are greater

1 population risk consequences of those types of
2 decisions.

3 Then finally, I guess we'll want to consider
4 looking at how it is that first responders, for
5 example, decide that they are within the target
6 population, that they should begin to follow the
7 direction to begin taking it now. And I think
8 that's related to their perception of risk. And
9 there are ways to assess risk perception, and we
10 should consider building those into the study as
11 well.

12 DR. MOORE: Very good. Ms. Young?

13 MS. YOUNG: Yes. I'd suggest that we do
14 follow-up studies on the psychological effect of
15 providing the kits to a specific population and the
16 potential demand that might come from the rest of
17 society, and what we do about that.

18 Then also, I would feel comfortable, given
19 that resistance in general infections in the
20 community is a concern, having a microbiology panel
21 of experts, of microbiologists, who can look at
22 that specific issue based on these use studies that

1 come out and the various scenarios that might
2 present themselves.

3 DR. MOORE: Dr. Hilton?

4 DR. HILTON: I wonder if it's possible to
5 have a mathematical model to study the tradeoff
6 between anthrax exposure without treatment and
7 widespread doxorubicin treatment of a population in
8 the emergence of resistance to antibiotics use. I
9 mean, we could trade one disaster for another.

10 DR. MOORE: Exactly. Well put.

11 All right. Well, with that then -- I'm
12 sorry, Dr. Walker. Go ahead.

13 DR. WALKER-HARDING: Just one quick thing.
14 It seems like some of the concern is how long it
15 lasts. I would think it might be nice to begin to
16 look at how to make doxycycline last 10 years; how
17 can you formulate it so that it's a 10-year
18 expiration date or whatever, but a longer
19 expiration date than it is?

20 DR. MOORE: Sure.

21 Well, with that, it appears to be the end of
22 the discussion and comments for question 2. Let's

1 move on, then, to question 3.

2 So the doxycycline medkit proposal includes
3 instructions for dosing children and adults who
4 cannot swallow pills to using the 100-milligram
5 tablets. So please comment on any additional
6 recommended studies to evaluate the dosing
7 instructions in this population.

8 I guess I'll go first. The easiest thing to
9 I think assess -- and you have to -- well, would be
10 to include a syringe, a pre-dosed syringe for
11 children, again taking into account what the cost
12 would be and feasibility.

13 But I guess the recommendation would be to
14 either include a syringe in the medkit or to have
15 the doxycycline issued as a liquid. It may be too
16 difficult, I would imagine, to do both, to have the
17 Strategic National Stockpile carry both. But
18 perhaps the syringe might be the easiest option.

19 Dr. Walker? Sorry. She's going to go and
20 then you.

21 DR. WALKER-HARDING: One of the things, just
22 logistically working with kids, you were saying you

1 can use syrup, whatever. I was asking what simple
2 syrup is; I had no idea.

3 [Laughter.]

4 DR. MOORE: I don't know, either, actually.

5 DR. NEILL: Come to Kentucky on the first
6 Saturday in May, and I will introduce you to the
7 elixir of the gods.

8 [Laughter.]

9 DR. WALKER-HARDING: But the thing is,
10 that's sticky. And you use that syringe one time,
11 and maybe you don't have time to clean it. People
12 lose their syringes. I do think it would be really
13 nice to really give that a lot more thought, you
14 know, Landis, how she's talking about how is this
15 packaged, because in reality, one syringe with
16 syrup, and chocolate milk, and all kinds of things
17 on it may not really last for even three days.

18 DR. MOORE: Fair enough.

19 Ms. Landis, do you want to say something?

20 MS. LANDIS: For those of you that don't
21 know, simple syrup, we usually compound with it in
22 the pharmacy, and it's pretty much like it sounds.

1 It's a sugary fixed syrup.

2 DR. NEILL: One to one water and sugar.

3 MS. LANDIS: Yes. And no, we don't put
4 anything fun in it like they do in Kentucky.

5 DR. NEILL: Maker's Mark is a lot of things,
6 but it's not funny. It's a very serious business.

7 [Laughter.]

8 MS. LANDIS: Okay. So noted. And I think
9 the other products they had there, when you list
10 chocolate milk, it just goes against the grain of
11 what I'm telling patients all the time, is not to
12 take it with dairy products. So there's so much
13 about this whole pediatric piece that I find
14 bothersome because they can go on the internet if
15 they want to, and they can see that it says don't
16 take it with dairy products. And then we have this
17 FDA piece that comes out and says, "Take it with
18 chocolate milk." So you're setting us up for doing
19 a lot of explaining to people that's not
20 necessarily.

21 You shouldn't be doing simple syrup.
22 There's no need for that to be in a kit. But

1 there's a lot of different flavorings that are out
2 there, even if it's a Kool-Aid packet. I mean,
3 look at something that is dry, crystal, or
4 whatever, that could be in an individual unit of
5 use or maybe it's in a small -- put a couple drops
6 in. Almost every pharmacy has Flavor RX. They can
7 flavor, and patients pay extra money because they
8 want their kids to take the medicine.

9 Look to them to see what kind of flavorings
10 make the most sense and put it all in one package.
11 Get rid of the teaspoons, number one, because we're
12 past that. Let's go with mLs. That's what we're
13 educating people on. That's what we try to put on
14 the prescriptions to help people understand what is
15 an appropriate dose and get away from the old
16 household.

17 Number two, put everything in the package so
18 that you can make it really easy. If there really
19 was an emergency, people are not going to be out
20 looking for bowls and a metal spoon, and trying to
21 get all this stuff up. Have a clear, plastic
22 bottle that has a marking. Put the water up to the

1 marking. Crush the pill. Put it in, flavoring.
2 Shake. Syringe fits on top. You can pull it out.
3 You still have a way to storage for the next dose
4 if necessary. Make it simple for the general
5 public. Let's not make it complicated. And again,
6 focus groups will get you that.

7 DR. MOORE: Dr. Kaplan?

8 DR. KAPLAN: I agree with all your comments,
9 but I also think we have to get down to basics.
10 John Bradley mentioned it. And we've been talking
11 about this for a long time, pharmacokinetics of
12 this drug in kids using current techniques. One of
13 the thoughts was to do these in areas where Rocky
14 Mountain spotted fever is a concern because every
15 child with a fever and even any kind of rash is
16 going to be put on doxycycline.

17 So there's all kinds of opportunities to
18 look at all these issues with respect to flavoring,
19 absorption, does chocolate milk interfere with
20 absorption. I think it needs to be studied, and I
21 didn't get the feeling that it was. And I wasn't
22 even sure who did the flavoring test. There's all

1 kinds of information on how it tastes great for
2 adults, but the kids don't like it. So maybe it
3 was studied in kids. I'm not sure.

4 DR. MOORE: Maybe they're very immature
5 adults.

6 Dr. Parker?

7 DR. PARKER: I think if it does move
8 forward, which I don't think it should -- but if it
9 does move forward and there is a further look at
10 how it happened in terms of answering the question
11 about studies, currently, for children who are able
12 to -- the parents are able to know -- or the person
13 taking care of them is able to know that they weigh
14 12 pounds or less. you're asking them to take
15 17.5 mLs separated by 12 hours.

16 So you need to really look at people's
17 ability to give a child that weighs less than 12
18 pounds 17 and a half mLs twice a day or every 12
19 hours for 60 days. Look at the accuracy and also
20 look at what that means in terms of safety and
21 efficacy.

22 So that would be very specific. Same thing

1 when you go to the 13- to 25-pound child. You're
2 then up to asking them to take -- that would
3 be -- then you're up to 1, 2, 3, 4. That would be
4 doing 20 mLs twice a day. And just sort of the
5 logistics of giving a child that size, that amount
6 of medication, twice a day for around 60 days, what
7 does that really mean when you come to actual use?
8 I think maybe the pediatric folks could weigh in on
9 that as well, not to mention what it tastes like.

10 My understanding, too, was the stability was
11 a 4-hour thing. And I see here, you can put it in
12 the refrigerator, put your label on it, and it's
13 24 hours. So I'm not clear which one's right.

14 DR. MOORE: Good point.

15 Dr. Neill?

16 DR. NEILL: The epidemiologic data that we
17 do have from the natural experiments that have
18 occurred with anthrax are concerning in as much as
19 it's not clear that kids respond the same way to an
20 exposure that adults do, for whatever reason,
21 having been exposed to exactly the same exposure.

22 Having said that, although this question

1 here is about studies to evaluate the dosing
2 instructions, since we're talking about a medkit
3 for children of first responders who may or may not
4 be in an exposed area, depending on where they
5 live -- whether Mom's going off to work as a first
6 responder, Dad's going off to work as a first
7 responder -- and knowing how difficult it is for
8 some of my parents to agree with the concept that
9 my giving a vaccination for, fill-in-the-blank
10 here, would be helpful and effective, I would
11 encourage the sponsor to consider studies that look
12 at the equivalent of the vaccine information sheet
13 that's included with vaccines for something like
14 this in prophylaxis for kids.

15 But I can tell you, as a primary care doc,
16 when that first responder calls me in advance,
17 saying, "I've got this kid at home," if something
18 is used -- or calls me in the event of an urgency,
19 I would be hard-pressed to suggest that the benefit
20 of administering to the child, especially if
21 distantly exposed, is going to outweigh any
22 potential risks. It's very clear there is no

1 science to support that assertion. Having said
2 that, there's a lot of inertia behind the -- or
3 rather, momentum behind the use of antibiotics as a
4 cure for everything that has an infectious bent.

5 So we include a MedWatch paper and all these
6 other -- there are like 10 different papers in
7 there. I didn't even undo it because I didn't want
8 to read through them all. But something in there I
9 think needs -- please consider a study of something
10 that would make my conversations with patients
11 easier in terms of that uncertainty, or just
12 reconsider dosing for kids at all.

13 DR. MOORE: Thank you. Dr. Gellad?

14 DR. GELLAD: I would like to echo I think
15 what maybe Dr. Day said before. I don't remember.
16 But when you pull this out, this is the first thing
17 you see, and it's all about the supplies and
18 everything. And this is only for those who need to
19 mix. And I think that's a real problem because the
20 part about with food and children who cannot
21 swallow pills is really small. All I see is
22 emergency, mixing doxycycline. So I think that

1 needs to be worked on.

2 The other point I wanted to make -- and this
3 is not specific to children, but it is because it's
4 about mixing -- is although this is an emergency,
5 we're not talking about something you have to do in
6 five minutes. I mean, I think that also needs to
7 be mentioned and that there's a lot of time,
8 actually, to put this mixture together. It's not
9 like putting an EpiPen in your leg.

10 So I just want to make the point that people
11 will have time to put these preparations together
12 if they need to. And that should be emphasized in
13 the instructions.

14 DR. MOORE: Yes. Dr. Reidenberg?

15 DR. REIDENBERG: I suspect that there is a
16 lot of information in part of the prescription
17 pharmaceutical industry dealing with pediatric
18 formulation, instructions, and so on. And I'm not
19 sure how much the sponsor has tried to get people
20 with this knowledge in the industry to advise them
21 on some of these issues. If they haven't, they
22 ought to consider getting advice from the people

1 who make these formulations regularly and have done
2 a lot of research finding out how to do it and what
3 works.

4 DR. MOORE: Dr. Neely?

5 DR. NEELY: So as a pediatric infectious
6 disease specialist, I look at that. I haven't seen
7 it since this morning, but as I recall, it was a
8 two-step dilution to get to the dose for somebody
9 like a child. And even if you were to do it
10 "perfectly," there's still a large error in there.

11 This just gets back to my original point for
12 question 1, that I think there probably needs to be
13 done a study looking at the efficacy, for lack of a
14 better term, and pick several outcomes, including
15 the accuracy of the dose given to children,
16 comparing home use versus using the pharmacies as a
17 point of distribution, because if you use the
18 pharmacies, you can have the pharmacist do the
19 compounding in a standardized way.

20 So I understand. I think it's probably too
21 difficult or too much to expect national stockpiles
22 to have enough liquid formulation and pill

1 formulation to supply the population. So if they
2 can focus on the pills, but have a very
3 standardized way of compounding so that families
4 that have children or other people who need liquid
5 get a formulation that's already made, tailored for
6 them, using a standard approach that they don't
7 have to compound, I think that's going to be a
8 better model. So I really think we need to have a
9 study that looks at pharmacies as a point of
10 distribution, comparing it to the home.

11 DR. MOORE: Dr. Huntley, and then
12 Dr. Walker?

13 DR. HUNTLEY-FENNER: So how much detail do
14 you want?

15 DR. MOORE: We have 35 minutes to go over
16 this and the next question, so I think we're okay.

17 DR. HUNTLEY-FENNER: Oh, that's helpful
18 guidance. It may make sense -- first of all, I
19 think someone suggested a while ago that you
20 consider having a mixing container and including
21 that in the kit. I think that's a very helpful
22 suggestion. And probably it makes sense to put the

1 syringe and that container in a separate bag and
2 says, open if you fall into that pediatric or
3 dysphagic category, whatever language you want to
4 use there.

5 Probably there ought to be some kind of
6 informed, I think, consent, if you will, for the
7 parent who is doing the compounding; that is, they
8 should have read the side effects page before they
9 began this process of mixing for their kids, so
10 they can better weigh the risks-benefits, because I
11 think we would all be hard-pressed to say that it's
12 an easy call under every situation. And separating
13 out the pediatric/dysphagic packet, I think would
14 help in that regard.

15 I do think that there's some work that can
16 be done with the graphics, and they probably ought
17 to be tested for comprehension, just having seen a
18 bunch of these. I won't go into detail there.

19 We ought to consider having something along
20 the lines of video instructions available online.
21 Remember that you aren't necessarily going to be
22 limited to what's in front of you on the written

1 page. There may be a place you can go that has
2 multi-lingual forms, videos showing exactly the
3 mixing process, someone going through all of the
4 steps. I mean, all those things I think are
5 potentially helpful to somebody who is flummoxed.
6 And as someone else said, you do have time. And
7 I'll stop there.

8 DR. MOORE: Dr. Walker?

9 DR. WALKER-HARDING: When we're talking
10 about how do you best give this to possibly
11 millions of people, hundreds of people, and we're
12 talking about this method, no matter how we do all
13 these -- give them three syringes, two
14 bowls -- different things, there are going to be
15 problems because they have to do all this mixing.

16 There are so many amazing ways we can make
17 medicines now, like dissolvable pills. I mean, why
18 can't we have a dissolvable pill? You put two
19 pills in half a cup of water. That lasts. Then
20 you pull out a certain amount, or you put it under
21 your tongue because there isn't any water and it
22 dissolves easily.

1 I think if we really wanted to do this well,
2 we would think a little bit more about completely
3 better vehicles that exist to dispense it besides
4 using pills that are already made, and dissolving
5 them, and crushing them. You don't have to crush
6 pills. We could have dissolvable pills. Then that
7 cuts out at least two of those things that you had
8 to deal with, the two bowls.

9 So I just think if we are really making a
10 good effort and this is affecting lots of people,
11 looking at a whole different way of packaging the
12 medication should be in order.

13 DR. MOORE: I'm sorry. Dr. Gellad?

14 DR. GELLAD: Just a quick question. In
15 terms of palatability, is it -- I guess I don't
16 know the answer to this. But these instructions
17 say that I will need one of these three foods in
18 order to administer this product to my child. So
19 can I administer it just with the water and
20 medication mixture?

21 So I guess the question is, do you need one
22 of these foods to supply this medicine? In other

1 words, am I going to need to go out to the store
2 and buy these things if I want to give this
3 product? Because it says here that I will need one
4 of these three foods to make this product. So just
5 as a parent I guess, I'm asking that question.

6 DR. MOORE: So you're saying that you'd like
7 to have some statement that it's okay to give with
8 water, and it may enhance --

9 DR. GELLAD: I mean, maybe you could test
10 this in the comprehension. I understand it, but
11 maybe some people will think that you need these
12 three in order to make it effective, rather than
13 just palatable.

14 DR. MOORE: Fair enough.

15 Dr. Neely?

16 DR. NEELY: Just to address it, it's going
17 to taste terrible. And so that gets to yet another
18 point about home use for kids. I guarantee you
19 that half of the kids are going to spit it out.
20 And then what's the family going to do? They're
21 going to try it again. Maybe they're going to spit
22 it out or they're going to wonder, did they get all

1 of it? Should I put more in? Or they may run out
2 of stuff. I mean, I think this is a bad model.

3 DR. MOORE: Okay. Point's well taken.
4 Let's move on, then, if there's no further
5 discussion, move onto the last question,
6 question 4.

7 So doxycycline is available in other dosages
8 and as liquid formulations. Please discuss the
9 pros and cons of the home preparation mixture
10 versus other available formulations for use in a
11 medkit.

12 Now, we've kind of already discussed this a
13 little bit, but if there are additional comments, I
14 would love to hear them.

15 Dr. Vaida.

16 I'm sorry. Dr. Morrato. Did we miss you on
17 the last one?

18 DR. MORRATO: Yes.

19 DR. MOORE: I'm terribly sorry.

20 DR. MORRATO: You got me going as a mom on
21 the food thing.

22 [Laughter.]

1 DR. MORRATO: So I don't know what simple
2 syrup is, either, so I think whatever gets in there
3 needs to be very clear about that. And I don't
4 understand why applesauce wasn't considered,
5 because that's commonly used to be mixing. So
6 anyway -- whatever foods it definitely shouldn't be
7 in, should also be included. Right? So if it
8 definitely shouldn't be in peanut butter -- or
9 whatever is critical from that bioavailability, I
10 think should be in the label, too.

11 DR. MOORE: Dr. Neely, do you want to say
12 something about simple syrup? I'm teasing. Go
13 ahead.

14 DR. NEILL: Again, on the first Saturday in
15 May, I will have everything I need to say about it.

16 With regard to this question, for children
17 of first responders, the mechanism that I would
18 likely employ -- were they to come with all of
19 these questions, what do I do, how do I, can I mix
20 it up, given that they're going to have to do it at
21 some point in the future -- is simply to write out
22 a prescription.

1 It would be helpful if there were liquid
2 formulation, some other formulation available with
3 this kind of, what I look at as, OTC dosing
4 information. We just went through the Tylenol
5 relabeling thing a couple of meetings ago. And
6 having that available in a palatable liquid form
7 that stays at the pharmacy, is used already -- I
8 feel like first responders, most patients would
9 feel "protected" if that initial step of getting a
10 prescription was out of the way. All they've got
11 to do now is find a pharmacy and then find it.

12 It's clear that the logistics, in the event
13 that that needs to be used, would have to be worked
14 out. You have to have it available, et cetera.
15 But it would make me more comfortable than all of
16 this that's in the kit now.

17 DR. MOORE: Okay. Thank you very much.

18 Dr. Vaida?

19 DR. VAIDA: Yes. Our organization, as
20 hopefully many of you know, has a national errors
21 reporting program. And when we go into ambulatory
22 centers or hospital and we talk with trained

1 healthcare professionals, it doesn't matter if it's
2 a pharmacist, nurse, or physician from our
3 organization. If we see anyone compounding or
4 preparing commercially available products, we tell
5 them to stop doing that because we get errors
6 reported whenever you add steps.

7 So I think, in the bigger picture, once
8 again here, I don't know if I'd spend any money on
9 looking at any of this when there's a commercially
10 available suspension and also a powder available.

11 I mean, this is something that, really, even
12 with the expiration dating -- even if you had to
13 put separate products, or even with the questions
14 on even having a medkit, this is something that I
15 really don't think you should look at with all the
16 discussion we had about how hard it is to compound
17 when we recommend not even healthcare professionals
18 compound products that they don't have to compound.

19 DR. MOORE: Thank you. Ms. Landis?

20 MS. LANDIS: I have never seen the liquid
21 products on my shelf, other than achromycin V from
22 a long time ago, which was a tetracycline mixture.

1 So having the PD bottles that are ready to go is
2 beyond my practice as a community pharmacist, so
3 I'm not sure where they're at. And, obviously,
4 it's not anything that's being used. I would
5 rather possibly look at -- and not only that, but
6 when you get into the pediatric suspension
7 products, cost is a big factor and short dating
8 also comes with it.

9 So you'd be looking at very short dating.
10 You'd be looking at increased cost to the patient
11 for those particular products. You'd also be
12 looking at, most of them, once they're
13 reconstituted, have a very short life, maybe
14 10 days, possibly 14. It just depends on what the
15 product is. So that means that they would be going
16 back again and again for that total 60 days to get
17 antibiotics to cover for their child.

18 I would rather see is there any differential
19 as far as studying the longevity of, say, the
20 doxycycline in a capsule form. It comes in tablet
21 and capsule, which would make it a lot easier if
22 the capsule could be just put in a container

1 without having to worry about the crushing of the
2 tablet, is there a lot of difference between the
3 longevity, the expiration dates, and the usage for
4 that.

5 Go as simple as you can. Again, we don't
6 want to make this a super-expensive product, but
7 let's make it easy for those. I don't know if the
8 pharmacist actually has to go in and compound each
9 and every one of these if you make it simple
10 enough. And there's a lot of times we have people
11 that are traveling or whatever, so we may even have
12 them have the prescription powder go out for an
13 antibiotic, and then we also measure out the amount
14 of water that they will add to that, with
15 instructions on how to mix it.

16 People do really well with that. I think,
17 if you enable people and you educate them, that
18 they're able to perform those tasks. And I think
19 that's a piece that's going to be really important
20 with this kit, to be sure that it's utilized
21 appropriately for their patients. And again,
22 trying to get in some kind of flavoring that's

1 included in this kit would certainly help do away
2 with the pictures that we have, as far as what you
3 need to have in your house.

4 DR. MOORE: Thank you. Ms. Young?

5 MS. YOUNG: I would also like suggest some
6 cost benefit studies of the refined program that
7 will have to come out of all of these studies that
8 are being done. Obviously, there are a lot of
9 refinements that will have to be made to make it
10 palatable, so to speak. So cost benefit of this
11 program versus others that are probably going on
12 within the security community, whether it's masks,
13 whether it's vaccines, and other things we'd never
14 think of, the cost benefit of this particular
15 program versus others that would actually have
16 similar effects.

17 DR. MOORE: Okay. I believe that may do it
18 for the discussion for today unless there are some
19 other questions or comments. I want to thank
20 everybody for their time and attention to this
21 important matter. I want to thank the FDA, and the
22 sponsor, and the responders for their time and

1 effort on this matter as well. Thanks very much.

2 Does the FDA have any last messages,
3 questions?

4 DR. LAESSIG: We just want to thank everyone
5 again. It was a very good meeting, and we
6 appreciate everyone's attendance and valuable
7 input. So safe travels if you are leaving today.
8 And otherwise, we will see you back here tomorrow.

9 **Adjournment**

10 DR. MOORE: Fair enough. Thanks again.

11 (Whereupon, at 4:34 p.m., the meeting was
12 adjourned.)

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